THE EVALUATION OF CERVICAL CANCER SCREENING PROGRAMMES

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BACKGROUND NOTE

This project describes the development and application of a series of computer programmes which have as a final objective the simulation of screening programmes for cervical cancer. For convenience, this set of programmes is referred to as the «IARC Model», the name deriving from the author's place of work at the time of submission of this project description, although some of the earlier work was undertaken whilst the author was employed by the Leeds Area Health Authority.

Several colleagues have contributed to the work described here, and their contribution is recognised in the Acknowledgements.

The project developed from work which began in 1977 with the objective of defining the precise patterns of screening activity in the Leeds and Wakefield Areas of Yorkshire, and calculating parameters of the natural history of cervical cancer. A research grant from the DHSS was awarded for this study from April 1978 - March 1980, with the author as principal investigator. During this period, an extension of the original research proposals was accepted - the use of the data collected in a simulation model of screening. The period of the research grant was thus extended (until November 1980), and Dr A.D. Clayden joined the author as co-director of the project with Mr P. Hodgson as research assistant, from June 1979 onwards. A report of this project was prepared for the DHSS in May, 1981 (The Yorkshire Cervical Cytology Screening Project. Final Report), and described the development and application of a simulation model based on that of Professor E.G. Knox, and the outline of a design for a microsimulation model. The development of the microsimulation design derived from a considerable volume of published work (described in section III), principles of design of clinical trials, the experience of Dr A.D. Clayden in modelling techniques, and programmes written by Mr P. Hodgson.

After the author's move to IARC in Lyon, a new version of the microsimulation model was developed. Mr P. Hodgson was employed as consultant in November 1981, and in consultation with the author developed a new programme (S1), incorporating some of the elements of the Yorkshire design, and at the same time many of the data files were changed and updated. During the following two years this programme has been extensively modified, and the version presented in Appendix 4 of this project description (S20) represents the 20th major revision. Most of these changes have been made by the author, but Mr M. Smans kindly assisted with the writing of some of the programme subroutines of S20 concerned with output tables. It is therefore no longer simple to identify the precise authorship of the 1800 lines of S20.

The programme GMTO.FOR (Appendix 1) is a distant descendent of the programmes developed by Professor E.G. Knox, but it has been much modified (mainly by the author, but also by Mr Hodgson), so that a precise attribution is difficult. Other programmes and their data blocks used in the model (e.g. Appendices 2,3,7) are entirely the work of the author.

The application of the Model in the formulation of parameters of the natural history of cervical cancer and the exploration of screening policies represents the author's own work, although discussion and consultation with various colleagues has naturally contributed to the ideas which have been developed, and the results presented.

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APPENDICES

ABSTRACT

There is now plentiful evidence from correlational and case-control studies of the effectiveness of cytological screening as a means of preventing cervical cancer. However, there is obvious disagreement about the form which screening programmes should take; the solutions recommended by different advisory committees vary widely. The choice of programme is governed (implicitly or explicitly) by cost-benefit considerations - how to achieve maximum reduction in incidence (or mortality) for the resources deployed.

Simulation models are a convenient and rapid method of exploring the outcome of differently formulated programmes, and of demonstrating the importance and interrelationships of the variables concerned. There are however two main disadvantages to this approach. The first relates to the imperfect state of knowledge about the natural history of cervix cancer, especially the ages of onset, rates of progression and regression, and distribution of sojourn times in the preinvasive and preclinical stages of cervical cancer. In practise, the different assumptions about natural history can lead to large variations in the apparently optimum programme. The second drawback is that many simulation models are either too simplistic or too abstract, so that verification of results against observed experience is not possible.

The model described reproduces the vital events and the population structure of England and Wales between 1961 and 1991. Onto this population is superimposed the natural history of cervical carcinoma, using data derived from several recent studies, so that the changes in incidence which are currently taking place can be reproduced. The technical solution adopted is a "microsimulation" - each individual in the population is retained as a unit - which allows factors such as disease onset and screening uptake to be dependent upon personal characteristics and past events. Screening can be offered as part of a routine programme, or incidentally - for example during pregnancy or hospital attendance.

The model allows quantitative evaluation of the complex patterns of screening activity that are currently observed in western countries. In addition, the relative importance of the different components of screening programmes, and assumptions about natural history can be studied. The model predictions can be compared with observed incidence and mortality from clinical cancer.

I INTRODUCTION

Carcinoma of the cervix was the first malignant disease for which programmes of mass screening were introduced. It is of course well known that this was done without the benefit of any evaluation of the effectiveness of the procedure. Perhaps it was regarded as self-evident that regular cytology examinations would be beneficial, but it is also the case that the need for evaluation of health care programmes was not widely recognised at that time (the early 1950's), and the problems peculiar to the evaluation of screening procedures were less well known. Whatever the reasons, the lack of any study involving longitudinal follow-up of women randomly assigned to different screening schedules has been a grave disadvantage in deciding whether the procedure is effective, and if so, how it should best be implemented in the community.

It is now clear that the incidence of invasive carcinoma of the cervix, and consequent mortality, can be reduced by the introduction of cervical cytology screening. The evidence upon which this statement is based is briefly reviewed later. However, there are clearly widely divergent views about the form which a programme for screening the female population should take. As in all decisions on the planning of health care, the ultimate point at issue is the most efficient use of resources. The relationships of the outcome of different screening programmes to the input of resources can theoretically be studied in experimental trials; however, in reality the number of possible screening policies which could be adopted is very great, and such trials would have to be very large and of very long duration to yield useful results. It is in such a situation that the use of simulation models is particularly useful in carrying out "simulated experiments" in a matter of minutes rather then years. It is becoming more usual to use this approach rather than relying upon entirely intuitive judgments when proposing screening policies. However, it has to be admitted that most of the models which are described in the literature are rather unconvincing; they are either rather elaborate mathematical abstractions designed to demonstrate the properties of sampling (screening) from populations with theoretical natural histories of disease, or their construction is so simplistic that it is difficult to examine all the factors relevant to the disease process or the screening programme.

This project grew out of an attempt to advise on a reasonable screening policy to adopt for a population of women in Great Britain. The nature of the evidence about the disease process, and the properties of the screening examination are first reviewed, and then the construction of a model which is

designed to study the outcome of screening policies in such a population over a short time period is described. The properties of the simulation model are demonstrated by using it to examine the outcome of very different, if rather theoretical, policies. The use of the model demonstrates the potential of this approach, and highlights the areas where the acquisition of more data is essential for the rational planning of screening programmes.

II CONTROL OF CERVICAL CANCER

1. EPIDEMIOLOGY OF CARCINOMA OF THE CERVIX

There are many excellent reviews of the epidemiology and natural history of cervical cancer, and it is not proposed to reproduce them here (see Rotkin, 1973; Walton et al, 1976; Cramer, 1982). Some of the factors that are essential to the later discussions on screening programmes will however be reviewed.

1.1 INCIDENCE AND MORTALITY FROM CARCINOMA OF CERVIX

1.1.1 International data

There are striking variations in the incidence of clinical cancer of the cervix in different parts of the world. Data is available for comparison from the volumes of Cancer Incidence in Five Continents. Fig 2.1 illustrates some of the large differences between age-standardised rates for the period around 1975.

Within these data there are variations in age-specific rates. Fig. 2.2 shows age-specific rates for the period around 1960 (when little screening for carcinoma of cervix was in progress). In the high risk areas there is a sharp increase in incidence after age 30 and a peak in the fifth and sixth decades. In lower risk areas the rise is more gradual, and a maximum incidence is in older age-groups.

In interpreting data from different centres it is important to bear in mind that there are potential sources of artefactual differences which are peculiar to cervical cancer. Firstly, the ICD classification system allows for the coding of "Uterus-unspecified" as follows :

ICD 6th & 7th revisions	ICD 8th revision
171 Malignant neoplasm of cervix uteri	180 Malignant neoplasm of cervix uteri
172 Malignant neoplasm of corpus uteri	181 Chorioepithelioma
173 Malignant neoplasm of other parts of uterus (incl. Chorioepithelioma)	182 Other malignant neoplasm of uterus
174 Malignant neoplasm of uterus unspecified	182.0 Corpus uteri
	182.9 Uterus, unspecified

ICD 9th revision

179 Malignant neoplasm of uterus, part unspecified

180 Malignant neoplasm of cervix uteri

181 Malignant neoplasm of placenta

182 Malignant neoplasm of body of uterus

The proportion of cervix cancers put into the unspecified category may vary considerably between centres. Secondly "carcinoma in situ" may be included in the figures for cervical cancer. This will certainly distort the age distribution of cases, and probably also inflate overall incidence. Thirdly incidence rates are presented per 10^5 women ; however not all women are at risk - hysterectomy is a very common operation and the prevalence of hysterectomy in western countries means that calculated rates will underestimate the true rates (per 10^5 at risk).

Mortality data is also available on an international basis. Table II.1 reproduces recent age-standardised (World population) mortality rates for 56 countries submitting figures to WHO (Segi et al, 1981).

Particular care is required in interpreting these rates, partly because of known under-registration of deaths in some countries, but also because of differential allocation of cervix cancers to the "Uterus-unspecified" categories as mentioned above. Once again it is clear that there are wide variations in mortality rates, which apparently vary at least eightfold in Europe, (between Spain and Denmark). Hill (1975) reviewed international mortality data, for uterine cancer as a whole. Table II.2 shows mortality rates for two time periods, and the probability of a decline in rates for cervical carcinoma. Evidence of decline has been of particular interest in evaluating the results of screening programmes (see section 3.2.3).

1.1.2 England and Wales data

The features of incidence and mortality from cervix cancer in England and Wales will be dealt with in this section, since some of this data will be used later in the simulation model.

Fig. 2.3 shows the age-specific mortality rates for cervix cancer for a recent period (1976-80); rates reach a maximum around age 55-60 and are then relatively constant.

Table II.3 shows mortality rates for 10 year age-groups for the period 1955-1980. The most interesting features in this table are the steady overall decline in mortality, especially since the early 1960's, but within this the recent increase in death rates among young women (aged under 35). At age 35-44 a decline occurred up until about 1974 since when the rates have increased. In the age group 45-54 there was a rise in mortality until 1968, since when rates have declined, and above this age the decline has been more or less steady. Hill and Adelstein (1967) pointed out that mortality rates varied by year of birth, and a more recent analysis is shown in Fig. 2.4. Mortality rates show a decline in successive birth cohorts up to the generation born around 1906, rise to a maximum for the 1921 cohort before falling to a minimum in the 1936 cohort. There has been a progressive increase in successive birth cohorts since then. These changes were attributed by Hill and Adelstein to increased risk of disease in women who passed the period of late teens and early twenties at times of social instability (wartime). The recent abrupt increase in young women has given rise to considerable concern (Adelstein, 1981).

Cancer registration data are available for the whole of England and Wales from 1962 onwards for invasive carcinoma of cervix, and for carcinoma in situ. Fig. 2.5 shows age-specific incidence rates for invasive cancer at four different time periods.

In Table II.4 are shown age-specific incidence rates for invasive carcinoma of cervix; these show trends very similar to the mortality rates, with recent rises in incidence in young women (under 35), a rise in the age-group 35-44 since 1974 and a fall at age 45-54 after a maximum rate in 1967.

The corresponding cohort curves are shown in Figure 2.6. There is a close similarity to the mortality curves; maximum rates are seen in the 1921 cohort and minima in that of 1931. There is a progressive rise in incidence rates in birth cohorts born since then. Some of the rise in incidence in young women might be attributable to the registration of micro-invasive cancers, discovered at screening, in recent years. Calculations based on possible numbers of such cases suggest that this can account for only a small proportion of this change, and a true increase in risk has occurred in recent generations. Part of the apparent bimodality of the age-specific incidence curves for 1976-78 (Fig. 2.5) is explained by the low rates at age 40-45 arising in women from the low risk 1931-36 birth cohorts. The remainder is probably due to the effects of screening (see section 3.2.3). The supposition

that such bimodality is caused by two distinct biological components of cervical cancer (Ashley, 1966; Hakama & Penttinen, 1981) is not necessary.

Registration rates for carcinoma in-situ are given in Table II.5. These rates will be dependent upon the number of smears which are taken - as this increases, so the number of positive cases will increase and the 'incidence' rate per 10^6 women will increase. In addition, completeness of registration is almost certainly less for in situ than for invasive cancer. Table II.6 relates number of smears taken (Roberts 1982 - see section 3.2.2) to the number of registrations and indicates that not only has there been an increase in the number of examinations, but the rate of positivity has shown an increase - especially under age 35. In view of the fact that with the progress of time a larger proportion of smears are repeat examinations on the same women, a reduction in proportion of positives might be anticipated. It is hard to escape the conclusion that there is a true rise in incidence of in-situ cancer in young women (Draper & Cook, 1983).

1.2 RISK FACTORS FOR CERVICAL CANCER

The factors which can be identified as being associated with increased or decreased risks of cervical cancer have been reviewed by Rotkin (1973), the Walton report (1976), Hulka (1982) and Cramer (1982). They are briefly summarized below.

Carcinoma of the cervix can easily be demonstrated to occur at increased incidence in urban rather than rural residents, in blacks compared to whites and in people of low social class compared to those of high. It is more common in married women than single, and in widowed or divorced women than married (Leck et al, 1978). The incidence of disease increases with the increasing number of pregnancies, and with decreasing age at first pregnancy. A variety of sexual behaviours are clearly associated with increased risk; early age at first intercourse, multiple sexual partners and a history of veneral disease.

It is clear that these variables are highly correlated - thus there is little or no independent effect of age at first marriage or age at first pregnancy when the relationships are controlled for age at first intercourse. Likewise marital status, number of marriages and history of venereal disease are related to cervical cancer via the directly associated variable of number of sexual partners. The importance of identifying directly associated variables rather than indirect or confounding factors is obvious if the focus is on the quest for aetiological agents. As will be discussed later, however,

it is less important when cancer control programmes are considered, when an indirectly associated variable, such as marital status, may serve to identify groups at increased risk of disease.

Various other variables have been postulated in the past as important risk factors, but their importance is now generally discounted; for example age at menarche, coital frequency and age at menopause. Circumcision of the male partner has been extensively investigated - the consensus view seems to be that if it is a risk factor it is a weak one, and is possibly related to penile hygiene. The possible role of the male partner in the disease aetiology is also suggested by associations with the social class of the husband, husbands whose jobs involve extensive travel, marital clusters of cervix cancer (cases in two or more wives of the same men) and concordance of cervical and penile cancer in married couples.

The role of contraception in aetiology is difficult to determine. Studies are particularly hard to design and interpret because the use of different contraceptive methods is closely related to the known risk factors for cervical neoplasia (sexual activity). In addition to this, contraceptive users are often subjected to frequent cytology testing during their attendances for family planning services; thus the chance of their being found to have preclinical disease is clearly much enhanced. Barrier methods of contraception appear to reduce the risk of neoplastic disease, but there is considerable controversy over the possible effects of oral contraception. Much of the early work was reviewed by a scientific group of WHO (1978). The Oxford Family Planning Study (Vessey et al, 1983) suggested that the incidence of neoplasia (all degrees, from dysplasia to invasive disease) was 75% higher in oral contraceptive users than IUD users, and that the relative risk was closely related to the duration of use. This is the most convincing evidence to date of a direct effect of steroid contraceptives on the cervix, but it is quite possible that the effects observed were the result of confounding by sexual factors.

The central role in aetiology which variables associated with coitus clearly play has suggested several causative mechanisms. Two factors associated with coitus itself are mechanical trauma and exposure to semen.

Coppleson & Reid (1978) suggested that there may be a carcinogenic factor in sperm, and Singer et al (1976) further suggested that this could be related to the seminal DNA interacting with that of the host to initiate epithelial transformation.

A more popular hypothesis to explain the link between cervical cancer and early intercourse/multiple partners is the possible role of a venereally transmitted infection. The candidate most frequently advanced as the responsible agent is the Herpes Virus type 2 (HSV2). There have been a number of studies which demonstrate an excess of antibodies to the virus in cervical cancer compared to controls : Table II.7 from Cramer (1982) summarises the results of ten such studies. In addition there are reports of herpes virus genetic material in cervical cancer cells (Frenkel et al, 1972; Aurelian, 1974) and the virus has been shown to have oncogenic potential in other species (Rapp & Duff, 1973). The evidence incriminating HSV2 as a possible causative agent has been consistent, and has survived attempts to explain the association as one confounded with other variables of sexual activity; it seems unlikely that much more light will be shed by further retrospective studies. Whatever its role the virus is almost certainly neither a necessary or sufficient cause of cervical cancer.

Recently it has become apparent that infection of the cervical epithelium with the human papillomavirus can give rise the cytological and histological picture of dysplasia in the absence of visible condylomata (Meisels et al, 1981). It is not clear whether this infection has become more common recently or, more likely, awareness of the rather subjective morphological features of viral infection has increased its recognition. It is unknown whether the dysplastic changes observed can progress to invasive cancer.

2. NATURAL HISTORY OF CARCINOMA OF THE CERVIX

2.1 THE NATURE OF PRECURSORS OF CLINICAL CANCER

Perhaps more has been written about the natural history of cervical cancer than about any other tumour. This is because the disease occurs in a relatively small area of squamocolumnar junction, and it is relatively accessible to examination. This availability to cytological and histological examination, and more recently the increasing use of, and experience in colposcopy, has permitted the identification of a series of sequential changes from normality to frank malignancy. Although the general pattern of such change is now accepted, there is controversy over the precise rates of change involved, and associated with this, the best nomenclature to use.

It was the widespread introduction of cytological examination of the cervix (with biopsy of cervices showing abnormal patterns) which led to the

identification of pathological conditions which were clearly related to carcinoma of the cervix. This latter connection was surmised not only on the basis of histological and epidemiological similarity, but as a result of early work which demonstrated that many of the lesions so discovered would progress with time to become clinically invasive cancer (Petersen, 1956). There was, moreover, quite a distinct morphological gradation amongst these precancerous intraepithelial lesions, ranging from a relatively slight disturbance of the epithelial structure to the presence of small anaplastic cancer cells. These latter lesions were termed "carcinoma in situ", whilst for those showing only slight morphological abnormalities the term "Dysplasia" came to be used. This latter is, then, rather a diagnosis of exlusion, being used for disturbances of differentiation not amounting to carcinoma in situ; it is, furthermore, frequently subdivided into mild, moderate and severe types.

These conditions are associated with the exfoliation of abnormal cells, and smears made from these cells show a continuous gradation of changes. This is a clear quantitative relationship between the histology of the cervix and the cytological appearances observed (Maisel et al, 1963), so that the latter may be reported in terms of the probable underlying histological changes. Alternatively the cytological appearance is given some kind of numerical grading, for example from I to V.

The validity of cytology and quantitative relationships between these pathological states (rates of incidence, regression & progression) are dealt with in more detail later (Section 2.3).

There seems no doubt that Dysplastic lesions can progress to in-situ cancer and similarly that regression to normality is possible (Stern & Neely, 1963; Fox, 1967; Richart & Barron, 1969; Sedlis et al, 1970; Nasiell et al, 1975). The more severe the degree of abnormality the more likely is progression and vice versa.

Carcinoma in-situ is clearly a precursor of invasive cancer, follow up of cases which are untreated is followed in a significant proportion by invasive cancer (Petersen, 1956; Kottmeier, 1953; Kinlen & Springs, 1978). Apart from direct follow up of in-situ cases there are other pieces of evidence suggesting that this condition is a precursor of invasive carcinoma. Thus carcinoma in-situ is frequently observed histologically at the margins of invasive cancer, retrospective examination of biopsies of women subsequently developing invasive cancer have been shown to demonstrate in-situ lesions (Galvin et al, 1952), and careful serial sections of biopsies of cases of

carcinoma in-situ has been shown to reveal foci of micro-invasion in up to a quarter of cases (Friedell et al, 1958).

The question of whether carcinoma in-situ undergoes spontaneous regression is more difficult to resolve because of problems inherent in the methods available. Cases followed by serial biopsy are subject to the therapeutic effect of the biopsy, cases diagnosed and followed by cytology only may have been false positive on initial cytology or false negative on follow up.
Koss (1970) maintains that spontaneous regression in the absence of treatment is a rare event. However, ethical constraints mean that there is now little prospect of resolving the issue from longitudinal follow up of untreated cases. The evidence available from population data suggest that the observed prevalence of cis cannot be explained other than by allowing for the probablity of regression.

The definitions of dysplasia and carcinoma in-situ already cited show that the distinction between them is entirely arbitrary. In order to emphasise this it has been proposed that the range of lesions be termed 'Cervical Intraepithelial Neoplasia' (Richart & Barron, 1969; Koss, 1978) with grading within indicated by the numerals I (slight morphological change) to IV (carcinoma in-situ). This has the advantage of emphasising the unity of these lesions, and from preventing a simple dichotomy of treatment of the patients so diagnosed on the basis of an arbitrary division. However, it adds very little to the understanding of the disease or the planning of screening, and when used below it is merely as a synomym for "both dysplasia and carcinoma in-situ".

2.2 RISK FACTORS FOR 'CERVICAL INTRAEPITHELIAL NEOPLASIA'

The relationship of dysplasia and in-situ lesions to invasive cancer is shown by the similarity of the variables which have been identified as risk factors. The usual method of study is by comparison of cases of CIN and matched controls who have been attenders at screening programmes. The results following are mainly from studies by Stern, 1969; Hulka & Zyzanski, 1971; Thomas, 1973; Cooper & Hillier, 1975; Harris et al, 1980; Sweetnam et al, 1981; Parkin et al, 1982a.

Although dysplasia and carcinoma in-situ are, by definition, preclinical lesions it has often been noted that their presence frequently coincides with gynaecological symptoms. This could presumably be due to the co-existence of CIN and other gynaecological abnormalities responsible for the symptoms, the

association being due to the similarity of the aetiological factors involved. Abnormal cervical pathology is associated with marital status, being more common in married than single women and more prevalent still in the formerly married, or those with a history of marital instability. Age at marriage and number of marriages are also associated factors. An association between parity (or gravidity) and CIN can usually be reduced by controlling for age and marital status (although the study of Barron & Richart (1971) in Barbados found an independent effect of number of pregnancies). Race (negro vs white), social class and variables connected with these (income, education, smoking) have also been shown to be linked to abnormal cytology or pathology of the cervix.

As with studies of the risk factors for clinical invasive cancer, there is a need to distinguish variables possibly linked closely with causative agents, and those which are confounding or secondarily associated. It seems that the same factors are involved, most of the variables being more or less related to coital practices, particularly early onset of intercourse, and multiple partners (Meisels et al, 1977; Harris et al, 1980).

Abnormal cervical cytology is noted more frequently than expected during pregnancy and the puerperium, and hence the rates of abnormality are higher than average in women attending ante and post-natal clinics (Parkin et al, 1982a).This may reflect the possibility that pregnant women are in higher risk categories (eg more sexually active) than the non-pregnant who attend clinics for cytological examination. It is generally held that pregnancy itself does not cause epithelial abnormalities, but the eversion of the endocervix provides a greater area for dysplastic change during or soon after pregnancy (Coppleson & Reid, 1966; Jones et al, 1968). Dysplastic changes noted during pregnancy may be relatively transient (Lurain & Gallup, 1979).

As in the case of invasive cancer, the role of contraception is difficult to determine. Increased rates of abnormality of the cervix are reported in users of oral contraceptives (Stern & Clark, 1970; WHO, 1978; Vessey et al, 1983) - however this may be related to sexual activity, and hence to reduced levels of abnormality in comparison groups. These latter may include users of barrier methods of contraception; diaphragm users have been shown to have low rates of preclinical abnormalities (Wright et al, 1978). The significant relationship with length of use of oral contraceptives found by Harris et al (1980) persisted after adjustement for number of sexual partners, and when users of the pill are compared with users of other non barrier methods of contraception. In this study, smoking appears as an independent risk factor.

The possible role of HSV2 in the aetiology of cervix cancer has been discussed, and Table II.7 summarises the results of case-control studies of positive serology; relative risks are higher for clinical disease than for CIN. An association between cervical pathology and Trichomonas infection has frequently been reported (Thomas, 1973; Parkin et al, 1982a). The association may be due to the more direct link of sexual activity, but it has been suggested that Trichomonas infection can lead directly to dysplastic lesions.

2.3 QUANTITATIVE RELATIONSHIPS IN THE NATURAL HISTORY

The evidence which has led to the general acceptance of the sequence of histological changes in the natural history of cervical cancer has already been described. It will become clear that such a general outline is quite inadequate if it is desired to influence the development of disease by intervening to interrupt this sequence - by a screening programme for instance. Planning such programmes demands quantitative data on the inter-relationships involved.

The type of questions involved are : -

- At what rate do histological abnormalities arise in the population ?
- How is this rate influenced by risk factors (age at coitus, first pregnancy etc) ? ie the size of the relative risk.
- What is the rate of development of the preclinical stages, and is this also dependent on factors such as age, parity etc ?

This last question, on rate of development, is a crucial one. The parameters of interest are really the distribution of sojourn times in the different preclinical states (dysplasia, carcinoma in situ, occult invasive cancer), and how these distributions are influenced by other variables. It is not surprising perhaps that the questions that have been answered (or, more accurately, for which answers have been proposed) are much simplified versions. Much effort has been expended to identify mean duration of these states, although this is a meaningless statistic without some knowledge of the range or shape of the distribution curve. Questions such as the percentage of carcinomas in situ which will eventually become invasive, or the percentage of

invasive cancers which do not appear to pass through an in situ stage are also merely indicating something about this distribution.

In studying the natural history, there are three methods which have been used to throw some light upon the natural history of precursor lesions.

1. The study of the life history of the lesions themselves in individual women (sometimes referred to as 'pathological evidence').

2. Inferring relationships between the different stages of disease from observations on cross-sectional rates of incidence and prevalence in populations. This latter approach requires the formulation of some kind of statistical model of the disease process.

3. The longitudinal follow up of women subjected to cytological screening to determine the rate of disease onset in those screening negative.

2.3.1 Studies of individual cases

The emphasis in such studies is to follow up a group of women with preclinical disease to determine outcome, and to quantify rates of progression or regression of lesions of differing grades of severity. A major drawback of such studies has been that the methods available either lack validity (cytology) or interfere with what is being observed (biopsy). Attempts to diagnose and follow up cases entirely by cytology have the problem of false positive and negative tests. It is impossible to decide whether transition from positive to negative findings represent a true change, or whether the first or second biopsy were false ! Attempts have been made to circumvent this by requiring several sequential smears to show the same cytological pattern before the 'diagnosis' is regarded as firm, but such a procedure precludes the possibility of detecting rapid fluctuations in disease status. The alternative approach requires that lesions are confirmed by histology of biopsy specimens; here the obvious critique is that the biopsy may remove the original lesion, or that the healing process following biopsy may also cure any adjacent preclinical disease. There is no way to adequately answer such critiques, even using modern methods of punch biopsy under colposcopic control, and the result has been a widespread belief that intra-epithelial neoplasia can never disappear spontaneously in the absence of external trauma.

A further problem in deriving quantitative estimates from such follow up studies is that the cases observed will not be representative of the pre-clinical disease which arises in a population, because of length-biased

sampling. For example, suppose that among incident in situ cases, 20% will progress to invasion in two years, 30% in twenty years, and 50% will remain unchanged (for, say, 40 years); then the relative likelihood that these three types will be detected by a single screening test is 2:20:40. The proportion actually observed will thus be 1.5%, 22.7% and 75.8% respectively - thus even though 20% of incident cases have a short in-situ phase, it appears from prevalent cases found on screening that this proportion is minimal.

Richart and Barron (1969) followed 557 patients with dysplasia. They found low rates of regression to normality, but their criterion for inclusion in the series was three consecutive dysplasia smears. This would certainly have the effect of enhancing the accuracy of the diagnosis of dysplasia (by eliminating false positives) but at the same time it eliminates the possibility of including patients with potentially transient lesions. Using various assumptions (transition independent of age, independent of time, no movement out of carcinoma in situ) they were able to estimate transition rates from dysplasia to carcinoma in situ; approximately 30% had so progressed in three years. The progression rates were closely related to the severity of the lesion, as judged by the grade of the smear class. These authors review the earlier literature on the outcome of patients with dysplasia. The majority of these studies make no reference to the time base involved, so that rates of progression or regression cannot be estimated.

Stern and Neely (1964) followed 130 women with dysplasia at intervals for up to 9 years by repeated cytology, supplemented by periodic punch biopsies ; criteria for diagnosis could be based on either. Because of the repeated examination, each patient could contribute more than one interval observation of progression and/or regression. They calculated progression rates from dysplasia to carcinoma in situ of 6.4% per year, with higher rates of progression in women under 45 years of age than those over 45. They also noted high rates of regression (32% per year) but recurrence was common in this group (33% per year). The authors note that these results would be markedly dependent upon the failure to observe dysplasia cells during follow up examination (false negatives) giving rise to apparent regression and subsequent recurrence.

Hulka (1968) followed 480 women with 'atypical' cytological smears (which were claimed to represent the pattern seen in mild/moderate dysplasia) and noted that in periods up to 12 months 51.8% apparently regressed to cytological normality whilst 14.2% progressed to 'suspicious' (representing severe dysplasia, carcinoma in situ or invasive cancer). The results of the

same series are presented in somewhat more detail in a later paper (Hulka & Redmond, 1971). Rates of progression are not constant with time, but are high during the initial period of follow up (6 months) and thereafter progressively fall. Progression rates are also influenced by age (higher at ages 30-44 than in younger or older women) and increase with increasing parity. Progression rates were higher in atypical smears found at the first screening (prevalent cases) than for those found during follow up of initially negative tests (incident cases). This seems reasonable if it is postulated that the prevalent cases would be at a more advanced stage of development, and that atypical smears preceded by one or more negative tests are more likely to represent transient lesions which regress spontaneously. The accuracy of the data produced is entirely dependent upon the ability of the cervical smear to reflect the underlying histology, and false positive or negative tests will markedly influence apparent progression or regression. The data produced by the authors suggests a far from perfect correlation between cytology and histology ; of the 99 cases apparently progressing from atypical to 'suspicious' cytology, 42 had either negative histology, or changes of mild/moderate dysplasia only.

Fox (1967) followed 278 women with cytological appearances of mild to moderate dysplasia (diagnosis being based upon a single smear). 86 apparently regressed (63 within 12 months) and 167 showed cytological appearances on follow up which necessitated cone biopsy, final diagnosis being 164 with severe dysplasia or carcinoma in situ.

In the series of 1712 cases reported by Nasiell et al (1975) mostly followed without biopsy, regression was observed in 64% of mild 'dysplasias', 54% of 'moderate dysplasias' and 43% of 'severe dysplasias', the mean follow up times being 2.1, 4.6 and 4.1 years respectively. The yearly probability of progressing from moderate dysplasia to severe dysplasia or C.i.s. was estimated to be 6-10%.

The fate of carcinoma in situ, if untreated, is even less well documented than that of dysplasia, since the former condition is usually regarded as sufficiently serious to demand complete excision (in the past this has usually been by cone biopsy, but treatment by laser has become fashionable more recently). Petersen (1956) in a well known series reported on 127 patients with histological appearances equivalent to carcinoma in situ followed up without treatment for a minimum of three years, after which period 11.4 % had progressed to cancer and 24% showed regression of histological changes. It should be noted that these patients had been initially detected because of

symptoms (and hence some may have actually had invasive disease not seen on biopsy), and that diagnosis and follow up involved biopsies which presumably would enhance the prospects of cure (apparent regression). The only British series to yield comparable information is that of Kinlen and Spriggs (1978) who followed 70 women with positive cervical smears (without distinction as to histological category) who had escaped biopsy for a minimum of two years. Ten patients had developed invasive cancer after a mean interval of 5.3 years. Biopsies were obtained from 53 of the remainder ; 19 showed regression to normal (this group was younger than the rest, regression was not observed over the age of 40) and a further three had micro-invasive carcinoma.

2.3.2 Population methods of estimating natural history

Several types of population data are available which can be used to derive estimates of natural history. The most widespread are mortality rates from carcinoma of cervix (from vital statistics systems) and incidence rates for clinical cancer of cervix which can be provided by population-based cancer registries. Information on the postulated precursor conditions (dysplasia, carcinoma in situ, preclinical invasive cancer) can only be derived from surveys of the population, which in practice means that they are derived from the results of screening programmes. The defects of this source of data are mentioned later.

The simplest type of inference made from population data has been to compare the mean ages of women found to have carcinoma in situ with the mean age of onset of clinical cancer, the suggestion being that the interval between estimates the duration of the preclinical lesion (eg Boyes et al, 1962; MacGregor and Baird, 1963). There are certain fallacies in such an approach. Firstly two different types of measure are being used - one is of onset (incidence) and the other of prevalence ; presumably the prevalent cases of c.i.s. would be at various stages in their evolution. The second problem is that the data sources are entirely different, and since the mean ages derived will be weighted by the age composition of these populations, the estimates of difference would be accordingly biassed.

The first clear statement of how population data can be used to derive parameters of natural history was made by Dunn (1953) and restated somewhat more clearly by Knox (1966) who also outlined the further studies that would be needed to provide such data.

It is necessary to point out at this stage that practically all population studies make use of cross-sectional data on age specific incidence and

prevalence to infer something about what might happen to individuals, or single cohorts of women. The fallacy of such an approach is well known in epidemiological reasoning. However the fact is that there are no data on a single cohort which might be used instead. The nearest approach to this is the British Columbia study (Boyes et al, 1982) which examines data from two birth cohorts observed over a 20 year period.

The second feature of such studies is that they all rely, implicitly or explicitly, upon some model of the natural history of cancer of the cervix. In general, in order to keep the number of parameters to those which can be estimated from available data, rather simplified models of the natural history have to be adopted. This is an acceptable approach provided that the data available from populations under study is compatible with the simple model to be used ; this is not always the case, as will be described.

The papers by Dunn (1953) and Knox (1966) outline how, if age-specific incidence and mortality of clinical cancer, and prevalence of preclinical stages are known, then some knowledge of incidence of preclinical disease means that the parameters of interest can be estimated. Dunn is mainly concerned with estimating mean duration of carcinoma in situ, and how this might vary with age, the necessary assumption being that all such lesions would ultimately progress to clinical disease. Knox on the other hand stresses the use of the data to estimate the proportion of in-situ lesions that progress (or regress), and also the proportion of invasive lesions that arise between screening examinations. This latter statistic in conjunction with estimates of mean duration would begin to indicate the information that is truly required, that is the distribution of sojourn times in lesions progressing to invasive disease.

At the time these papers were written there was little available data on the prevalence or incidence of preclinical carcinoma of the cervix. Knox's paper described the ideal study which could provide the data needed. This involved investigating a (preferably random) group of 100,000 women with three successive smears. The first examination would allow estimation of prevalence rates, whilst the second, carried out very soon afterwards, would allow error rates to be calculated and corrections made to the prevalence figures. The third examination, after intervals ranging from 1.5 to 2.5 years, provides data for estimating incidence. Not surprisingly, a study of such size and complexity has never been performed. Instead there are available results derived from screening programmes in various centres.

The first problem raised by the use of such groups is the non-random nature of the population examined. It is well known that women who attend screening programmes are not a random section of the female population, and many of the respects in which they differ are related to cervical cancer and its precursors (Section 3.2). It has been noted that quite a large proportion of women attending for cytology examination may have gynaecological symptoms (Parkin et al, 1982 a) ; if interest is in preclinical precursors of carcinoma of cervix then patients with symptoms due to such underlying disease (but not to other diseases) should be excluded - hardly a practicable proposition.

A second problem is that screening programmes are designed specifically to interrupt the natural history of cancer by identifying and removing possibly precancerous lesions. Studies of natural history have not always allowed for this; for example estimates of prevalence of preclinical disease will depend upon the previous intensity of screening in the population. In addition the phenomena of "length bias" (Feinleib & Zelen, 1969) means that, where the preclinical lesions concerned have differing rates of growth and progression, lesions which are detected in a population that is more or less unscreened will be relatively benign or slow-growing compared with those discovered during an ongoing screening programme.

Screening programmes involve cytological examination, followed by further investigation if the cytological pattern appears to be abnormal. The lack of validity of cytology as a predictor of underlying pathology of the cervix is fully discussed in Section 3.2.1. Estimates of numbers of pathological lesions present are based only on subjects with abnormal cytology, and will underestimate the true numbers since false negative cytology examinations will not be biopsied. Furthermore, attempts to infer the course of pathological abnormalities of the cervix by serial cytology examinations will be misleading to the degree that false-negative and false-positive tests will be included.

The extent of investigation of cytologically abnormal subjects is, in pratice, related to the degree of abnormality observed, so that women with apparently mild changes may be followed up by cytology alone, and may fail to attend such appointments. Since there is some correlation between cytological patterns and underlying histology, it is not safe to assume that the distribution of pathological changes in cytologically abnormal subjects biopsied vs not biopsied is the same. Nevertheless some such assumption must be made in practice.

PREVALENCE OF DISEASE

For reasons discussed, presenting prevalence data for populations subject to repeated screening is meaningless. Similarly crude rates - eg at all ages - are worthless since they will be highly dependant on the ages of the group examined.

Fig 2.7 and 2.8 show cross sectional prevalence data by age in previously unscreened populations, two British and three North American. The North American series and that from Yorkshire are based on women receiving first examinations in screening programmes, and that from Cardiff derive from the 65% of ever-married women in the city, previously unscreened, who accepted an invitation to be examined. None can be considered as a random sample, therefore. In all these studies. the method of determining the numbers of women with cervical pathology (smear test followed by confirmatory histology on those abnormal) leads to prevalence figures being in fact the prevalence of true positive tests. The true population prevalence can be estimated by dividing by the sensitivity of the test (see section 3.2.1).

The low rate of histological follow up in cases with only lesser grades of cytological change meant that the absolute values of the prevalence rates of dysplasia for Cardiff were of little value. Nevertheless those workers have produced particularly useful figures for the relative prevalence of different pathologies in different subgroups of the population (see Fig 2.9).

Only one study has attempted to estimate age-specific prevalence in birth cohorts. Boyes et al (1982) studied the results of screening on two birth cohorts (born 1914-18 and 1929-33) between 1940 & 1969.

Although in theory this should have allowed comparison between the rates of disease at ages 35-39 in the two cohorts, this in fact proved impossible since the women screened in the early years of the programme gave atypical results (they were often referred because of symptoms). Nevertheless the prevalence (and incidence) rates in adjacent age-groups were similar, which encouraged the authors to combine both sets of data as a single series.

Table II.8 shows prevalence data from this study, including the figures corrected for false negative tests (the method of estimation of false negative rates from this study will be described later). The figures for carcinoma in situ or worse include lesions which subsequently proved to be microinvasive or occult cancer ; however such cases were a minority (< 10% under age 40, 15%

over age 40) and the prevalence of c.i.s. is considerably higher in this series than in any of those shown in Fig 2.8. Conversely the prevalence of dysplasia is rather low. This may be largely due to the exclusion of smears showing mild (class 2) abnormalities which were not biopsied (not normal procedure during the study period) or followed up for long periods without resolution ; thus any true dysplasias likely to regress would probably have done so. Differences in terminology may also be present.

INCIDENCE OF DISEASE

Incidence of cervical intraepithelial neoplasia should be calculated from new cases occuring in a population known to be free of disease. Figs 2.10 and 2.11 present estimates of incidence of dysplasia and carcinoma in-situ in relation to age. The data of Dunn & Martin (1967) and Bibbo et al (1971) allow the calculation of rates of new true-positives in women with more than one previous negative cytology examination. However the rates of Fidler et al (1968) and Parkin et al (1982 b) are based on new true-positives in women "with at least one" previous negative cytology examination. If only one previous test has been performed, the population will contain lesions missed on that occasion (false negatives). Since at all but the youngest age groups prevalent cases are more frequent than incident the actual number of 'missed' cases may be quite high in relation to truly incident ones. Parkin et al (1982 b) comment that in their series the majority of women examined were likely to have had more than one preceding test, hence such bias was probably small.

The estimated incidence rates from the British Columbia cohort study (Boyes et al, 1982) are shown in Table II.8. Two approaches were used to eliminate the effect of false negatives from initial screenings artificially inflating incidence. The first involves calculating the rates using only the data least affected by false negatives (second smears 3 years or more after the first, 3rd smears with intervals over 23 months and subsequent smears with intervals over 11 months), the second uses estimated false negative rates to make the necessary adjustments.

In the context of using statistical models to derive transition rates between preclinical states, or to clinical disease, it is important to be certain exactly what is meant by incidence of carcinoma in situ. In all of the series quoted the calculations are based on new cases in a population known to be normal (assuming the problem of false negatives is allowed for). If a screening programme detects lesions at an earlier stage than c.i.s., and some form of therapy is instituted, the incidence rates for c.i.s. derived as above

cannot be usued to estimate the probability of progressing from normal to preclinical disease. Moreover, where more than one preclinical stage is recognised which are sequentially related, the incidence rates of each will be influenced by the interval elapsing between the first (normal) and second examinations. Population based data cannot be used to resolve the question of the proportion of dysplasias that progress to carcinoma in situ.

Fig 2.12 shows the relationship between prevalence of clinical/preclinical disease and incidence of preclinical lesions based on the British Columbia data of Fidler et al (1968). The lower curve is the cumulative incidence of clinical cancer (for British Columbia 1955-1957). Above this line is added the prevalence of in situ cancer detected on screening in 1960-66. (Age specific prevalence for micro-invasive and occult invasive disease is not given and may in fact be included in the in situ figures; even if not, these only make up about 10 % of preclinical carcinoma detected, so that the inclusion of these conditions would only raise the upper prevalence line slightly). The cumulative incidence of in situ cancer plotted on the same curve excedes the summed prevalence curves by a factor of about two. Superficially this suggests that only about half of the incident in situ cases will progress to clinical cancer.

Other possible explanations for this discrepancy exist. Firstly, because incident data was calculated in women having had at least one negative smear (rather than two or more), the presence of false negatives at the initial screening may have lowered prevalence and raised incidence rates. Secondly, it is possible that a cohort effect is present, that the younger women with incident in situ carcinoma in this population will suffer higher rates of clinical cancer in future.

A similar comparison was carried out by Dunn & Martin (1967) using data from the San Diego County cytology registry. These workers derive incidence and prevalence rates for dysplasia in addition to in situ and invasive carcinoma. Incidence of dysplasia and in situ disease once again greatly excede incidence of clinical cancer plus prevalent preclinical lesions suggesting that regression occurs, and they suggest that "one would feel intuitively that this would happen most frequently in dysplasia where histological commitment appears less certain". They noted that incident cases of in situ disease excede cases first appearing as invasive lesions in the ratio 10:1; this suggests that only a small proportion of in-situ disease progresses rapidly to invasion, but lack of suitable time data precludes accurate quantitative estimation.

Dunn (1953) pointed out that, regardless of the fate of the lesions, average duration can be estimated by the formula :

$$\frac{\Sigma \text{ Age specific prevalence rates}}{\Sigma \text{ Age specific incidence rates}}$$

The data of Dunn & Martin (1967) suggest an average duration of dysplasia of 3.8 years and carcinoma in situ of 8.1 years ; Fidler et al (1968), using the same technique, estimate average duration of carcinoma in situ to be 6-9.5 years.

The careful analysis of data from two cohorts of women examined in British Columbia shows that the gap between incident and prevalent disease cannot be explained either by carry over of false negatives or by a cohort effect (Boyes et al, 1982). In this study the ratio between prevalence of c.i.s. plus cumulated incidence of clinical cancer and the cumulated incidence of c.i.s. is 0.67 by age 47 (see Fig 2.13), and the proportion of c.i.s. that progresses to clinical cancer is 26% by age 50-53. (These figures are 0.86 and 53% if incidence rates are calculated from first abnormality rather than mid-point). Including figures for dysplasia leads to only a small increase in prevalent disease plus clinical cancer, but a large rise in the cumulative incidence (see Fig 2.13). This seems to imply that regression is particularly frequent in dysplasia.

Kashgarian and Dunn (1970) present data from the Memphis Shelby county screening project. The model of cervical cancer which they consider envisages progression from normal to atypia, to intraepithelial carcinoma, to preclinical invasive cancer and then to clinical invasive cancer. In the analysis of the data, however, cellular atypia is ignored. Prevalence of intraepithelial carcinoma and preclinical invasive disease in an unscreened population are presented (with some hypothetical reductions to allow for screening of women with symptoms of cancer ; although how such symptoms were defined is not stated). Incidence of in situ and preclinical invasive cancer are computed from new cases in women with two previous negative smears, and incidence of clinical cancer for some years before screening is presented. The age specific incidence rates of clinical cancer of cervix are 2-3 times higher than the British Columbia or England and Wales rates, and there was an extremely high prevalence of invasive cancer found on screening - indeed it was found more frequently than carcinoma in situ, the rates of which were similar to those in Fig 2.9.

The cumulative incidence of intraepithelial plus occult invasive cancer was quite close to that of observed clinical disease and prevalent cases except in the older age-groups (see Fig 2.14). It seems likely that the prevalence and incidence rates calculated for the older age groups are inaccurate because of small numbers and that computed rates of preinvasive disease are underestimates because of the removal of cases showing 'atypia' after the initial two screenings. Estimations of average duration from summed age-specific rates suggest in situ disease lasting 10.7 years, and invasive preclinical disease 5 years.

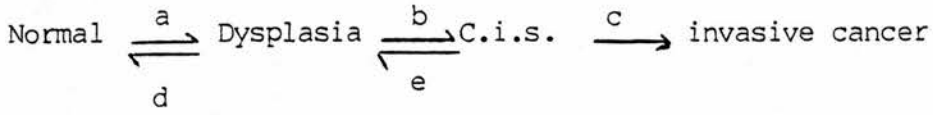
Barron & Richart (1970) present data on prevalence of abnormal cervical smears in a small population in Barbados. With two rather unlikely assumptions (that cytological grade represents underlying histology, and that regression of lesions is impossible) they point out that the relative prevalence of each grade of lesion would be proportional to its mean duration. The ratio of transit times so estimated was similar to that observed in their US follow up study (Richart & Barron, 1969).

In a later paper Barron et al (1978) use the British Columbia data of Fidler et al (1968) to estimate the duration of carcinoma in situ. Unfortunately the model of the disease process which is used by these workers involves a great many simplifying assumptions, so that the results quoted may bear correspondingly little relationship to reality (average duration of c.i.s. 3-10 years).

Albert (1981) describes a more complex model of disease which allows for regression of carcinoma in situ. He uses the British Columbia data in this model, and by what seems to be an iterative procedure produces best estimates for the transition rates of interest. Unfortunately details of the precise methodology are unavailable. The model ignores all abnormalities which may exist before carcinoma in situ, they are subsumed in the "Disease Free" state; it is thus highly questionable whether the British Columbia data on incidence of carcinoma in situ are appropriate (this is based on transitions from normal cytology to in situ disease). Moreover, since in reality dysplastic lesions are identified on screening and subjected at the very least to more intensive follow up than normals, the estimates of the proportion of occult invasive cancers which derive directly from the "Disease Free" state (1/3) are highly questionable.

The reason that simplified models of natural history have been so widely used is however clear when the results of trying to derive parameters for more

complex formulations are considered. Coppleson and Brown (1975) described the natural history thus : -



They used the data of Bibbo et al (1971) on incidence and prevalence of dysplasia and C.i.s. together with age-specific rates of invasive cancer from the US Third National Cancer Survey.

With five sets of transition rates to be derived it was not possible to determine a unique 'best fit' natural history using population data alone. Since the only transition rates which can be estimated from the data are normal to dysplasia (a), and c.i.s. to invasive cancer (c), there are a whole range of values for b, d and e which are compatible with the observed prevalences! Knox (1973) had already pointed out the same problem in describing his own simulation model, and employed several theoretical natural histories typified as either 'dynamic' (permitting high regression rates) or 'progressive' (regression rates minimal).

2.3.3 Longitudinal studies of screened populations

The only observational data likely to yield information of practical value is the follow up of participants in screening programmes to study the rates of onset of invasive cancer at varying intervals after a negative screening test (Walter and Day, 1983).

Immediately after a negative test, the incidence of clinical cancer is reduced to a level corresponding to the false negative rate of the test. There will then be a slow rise in incidence as cases with short preclinical sojourn times become manifest. If a second test is performed, the incidence cases thereafter will then consist of persons with two false screening results, those arising between the two tests with one false result, and new cases since the second test. Incidence data available after varying numbers of tests will thus allow estimation of the unknown parameters of interest : false negative rate and distribution of sojourn times prior to onset of invasion.

The essential data for this kind of study is the past screening history of women found to have invasive cancer, and relatively large numbers of subjects are required. No information will be forthcoming on the dynamics within the preinvasive stages - however from a practical point of view this is of much less consequence than modelling approaches which ignore the existence of early

lesions. In practice, some form of intervention, even if only a more rigorous follow up, is likely for such cases, so that the 'natural' history is, in effect, interrupted. In planning screening programmes the essential knowledge concerns the rates of development of all detectable preclinical lesions, and the test characteristics.

3. PREVENTION OF CARCINOMA OF CERVIX

3.1 PRIMARY PREVENTION

Primary preventive measures for disease take the form either of reducing exposure to risk factors, or increasing host resistance to them. Current evidence suggests that the most important risk factors are related to early onset of sexual activity and multiple sexual partners, possibly due to transmission of an infective agent (viral). It seems highly unlikely that any attempt to alter the sexual mores of society on public health grounds would meet with any success whatsoever. Experience in attempting to reduce cigarette smoking, where the relative risk of cancer is much higher, gives no grounds for optimism. Genital hygiene is sometimes cited as a potential preventive measure; apart from the imprecise meaning of this term, there is no evidence whatever that cleanliness, though desirable on many other grounds, would be preventive for cervix cancer. There is however some evidence, mentioned above, that barrier methods of contraception reduce the risk of precursor lesions, their use might be encouraged in preference to oral contraceptives especially during early sexual life.

The suspicion that viral infection plays a role in the genesis of cervical cancer has lead to hopes that the development of vaccines may allow prevention by increasing host resistance. It seems likely that a vaccine against herpes genitalis will be developed relatively soon, especially since this condition is becoming a major public health problem in the USA. There are many problems involved in evaluating the effectiveness of vaccines in preventing cancer, and trials would have to be very large (Higginson et al, 1971). Furthermore, herpes virus is almost certainly neither a necessary nor sufficient cause of cervical cancer, and complete protection from vaccination is highly unlikely, although incidence may well be reduced. The possible role played by human papillomavirus infection in the aetiology of dysplasia has been discussed in 1.2; a great deal more epidemiological and laboratory research on the carcinogenic potential of this virus is required before any trials of intervention could be considered.

3.2 SCREENING FOR CERVICAL CANCER

The description of the natural history of cervix cancer in section II.2 indicates the lengthy duration of histological abnormalities of the cervix which precedes the onset of invasive cancer. The development of the Papanicolaou technique for examination of cytological material obtained from the cervix provided a method which could be used for the widespread screening of women underlying abnormalities. The potential for prevention of invasive cervical cancer seemed so clear that widespread screening was gradually introduced in many countries in the 1950's and 1960's. There has been no formal evaluation of the effectiveness of screening, with the result that there has been a continuing debate as to its precise value (e.g. Knox, 1968; Foltz & Kelsey, 1980).

3.2.1 Screening tests and their validity

The available screening tests all aim to obtain cellular material from the cervix. This can be achieved by a cervical spatular scrape (usually with the knuckle-ended Ayre's spatula), or a vaginal aspirate taken with a cyto-pipette. The latter method seems to provide a poor yield of abnormal cells when compared to the scrape (Wied, 1955). The sole advantage lies in the fact that subjects can obtain their own specimens; however, this is more than offset by inadequate sampling, poor motivation and organisational problems of arranging follow-up (Anderson & Gunn, 1966; Reagan & Lin, 1967). The cervical scrape administered by trained personnel still fulfills the requirement of being a simple, cheap and acceptable method of sorting out the apparently diseased (who probably have the condition under investigation) from the apparently well (who probably do not). Screening tests are not intended to be diagnostic, indeed the frequency with which a test result is later confirmed by an acceptable diagnostic procedure is termed the validity of the test.

The results of a screening procedure can be conveniently summarised in the form of a 2 X 2 table (Thorner & Remein, 1961).

	TRUE DIAGNOSIS		
TEST RESULT	Disease	Normal	
Positive	a (true positives)	b (false positives)	a + b
Negative	c (false negatives)	d (true negatives)	c + d
	a + c	b + d	a + b + c + d (= N)

Frequently used measures of validity are the sensitivity of the test, i.e. its ability to yield a positive finding when disease is present ($^{a}/_{(a+c)}$ in above schema), and the specificity, the tests ability to give a negative result when disease is absent ($^{d}/_{(b + d)}$).

For some reason there is considerable confusion in the literature in reporting validity of cervical cytology screening. In addition to the above definitions, May (1974) proposed the following terminology : -

True positive rate (True prevalence)	$P = {}^{(a + c)}/_{N}$
True rate of false positives	$f_p = {}^{b}/_{(b + d)}$
True rate of false negatives	$f_n = {}^{c}/_{(a + c)}$
Apparent positive rate	$p_a = {}^{(a + b)}/_{N}$
Pseudo rate of false positives	$r_p = {}^{b}/_{(a + b)}$
Pseudo rate of false negatives	$r_n = {}^{c}/_{(c + d)}$
Apparent rate of false negatives	$r_{an} = {}^{c}/_{(a + b) + c}$

When the prevalence of disease in the population is relatively low, b + d will be quite close to N, and the false positive rate (f_p) can be approximated by $^{b}/_{N}$.

The true positive rate (p) cannot be deduced from the results of screening alone, which only produces an apparent rate of positives, Pa ($^{a + b}/_{N}$); however it is common for screening programmes to cite their results in this way, as the proportion of women examined who showed abnormal or suspicious cytology. In order to derive P, the number of true positives (or false positives) AND the number of false negatives (or true negatives) must be known, and these cannot be identified immediately but only after careful investigation and long term follow up. It is not correct to calculate false positive and false negative rates using the test results as the denominator.

The identification of false-positive results entails the follow up of subjects with positive cytological findings on screening. This is ideally done by histological examination of biopsy material, but for milder grades of cytological abnormality, follow up has often entailed recall for subsequent cytological examination. The results may be expressed as the proportion of positive smears which prove to be false-positive on follow up (the pseudo-rate of false positives, r_p), or as the predictive value of a positive cytology

test (1- rp). Although the true false-positive rate (fp) cannot be directly calculated, it is approximated by $^{b}/_{N}$, which is given by :

$$^{b}/_{N} = {}^{r}p \times Pa = (^{b}/_{(a+b)} \times (a+b)/_{N})$$

The value of Pa and rp are likely to be related, since the proportion of smears in a screening programme which are judged 'abnormal" is subjective, and depends on the proportion of borderline (class 2, dysplastic), smears which are so classified. Where smears with mild grades of cytological abnormality are followed up, a correspondingly high proportion will prove to have insignificant underlying pathology, or will be transient in nature. This is a specific example of the interrelationship of yield, sensitivity and specificity and the choice of cut-off points in screening tests. Data from screening programmes in Britain are given in the table below : -

Study	Cytology	Yield (Pa)	rp	Estimated fp
Manchester (Yule 1973)	Suspicious /positive	1.0 %	0.04 (46% biopsied)	0.04 %
Manchester (Husain 1976)	Dysplasia (or worse)	1.0 %	0.27	0.27 %
	Cis (or worse)	0.5 %	0.03	0.02 %
Brighton (Andrews et al, 1978)	"All abnormal"	1.5 %	0.08 (56% biopsied)	0.12 %
Cardiff (Evans et al, 1981)	Dyskaryotic (or worse)	1.4 %	0.19	0.27 %
	Suspicious /positive	0.8 %	0.04	0.03 %
Yorkshire (Parkin et al, 1982a)	Dysplasia (or worse)	2.9 %	0.32	0.93 %
	Cis (or worse)	0.4 %	0.13	0.05 %

Figures from British Columbia (Boyes et al, 1982) suggest false positive rates of 0.28 - 0.36 per 100 for dysplasia or worse, but on this study smears showing grade 2 cytology were only included if the changes persisted. If all class 2 smears had been included, the false positive rate would have been considerably higher.

False negative error in cervical cytology screening can arise in two different ways. The first of these is laboratory error, in which although abnormal cells are present in the smear, they are not recognised by the cytotechnologist. Laboratory quality control is aimed at reducing such error to a minimum. In practice its extent can be estimated by reviewing previous smears for women who have a detected abnormality.

The other component of false negative error is the absence of abnormal cells on the slide, even though a lesion is present in the cervix. This might arise due to non-exfoliation of atypical cells at the time of examination or to faulty technique in taking the specimen or making the slide. It is more difficult to measure, since this requires re-examination of a random group of women screening negative to determine how many truly had histological abnormality. Results are usually presented as the apparent rate of false negatives (^{r}an), and values of 5-30% are reported (see review by Husain, 1976), the finding in Manchester for example was 14.9% (Husain et al, 1974). As discussed by May (1974) the relationship between the true false negative rate (^{f}n) and ^{r}an is determined by the proportion of positive tests which are false positives (^{r}p). Using data from Sedlis et al (1964) he shows that an ^{r}p value of 70% converts an ^{r}an value of 30% to a true rate of false negatives of 59%. The data of Yule (1973) which includes an ^{r}p of 4% and a ^{r}an of 17.9% yields a true rate of false negatives of 18.5%.

A different approach to the estimation of false negative error was proposed by Knox (1966). Incidence is calculated from new cases arising in an interval following a negative screening test. However, in the presence of false negatives, these incident cases will be inflated by cases missed by the first examination. The shorter the interval between the tests, the greater the proportion of apparent incident cases which are "missed" false negatives. Furthermore, after several smears have been taken any positive case is likely to be a genuine new case, since the chances of a lesion being missed diminish on successive examinations. Data which present incidence rates based on second, third etc smears, and with different intervals between tests can therefore be used to estimate false negative rates. A necessary assumption in the calculations is that the chance of error is about the same at each examination, and is independent of whether an error has already been made previously. Coppleson & Brown (1974) used data presented by Christopherson (1966) and Koss (1970) on rates of histologically proved abnormality in a series of examinations on the same group of women. They calculated a true rate of false negative tests of 20-45%. Boyes et al (1982) used a similar method - however by reviewing the previous smears of new incident cases they were able to eliminate laboratory error, so their calculation on apparent incidence with different intervals and smear ranks provided estimates of the residual (non-laboratory) false negative error. This was 9.6% for cis (or worse) and 10.8% for dysplasia (or worse). There was a suggestion that the proportion of false-negatives decreases with advancing age. Their estimate of laboratory error was 8.5-15.5%, thus it seems that the overall false-negative rate is 20-25%.

3.2.2 Screening Programs

Screening programs which aim to examine whole populations of women have been introduced in a great many parts of the world. It is not possible to review these in great detail. The development of screening in England & Wales will first be reviewed, then some of the better known programmes elsewhere will be briefly described.

3.2.2.1 Screening in England and Wales

It is probably being rather generous to describe the development of cervical cytology screening in England and Wales as a national 'programme'. For the most part the services which have developed vary considerably from one place to another. Official policy was first described in 1966 (Ministry of Health, 1966) as allowing for the screening of women aged 35 and over at five yearly intervals, and Hospital Boards were made responsible for providing the necessary laboratory facilities. A standard form, HMR 101/5 (Fig 2.15) was provided as the basis of a recall scheme. This was of five-copy form, the various copies being retained by (i) the taker of the smear (ii) the subjects general practitioner (if different) (iii) the examining laboratory (iv) the health authority (v) the NHS Central Register. It was up to the latter organisation, which filed all forms received in chronological order, to operate a recall scheme. This was done by returning the copy relating to the original smear to the local health authority (usually the executive council/family practitioner committee) of the woman concerned, providing that no evidence of an 'interim' smear, within 5 years of the last, could be detected. The age for the first test was later modified to include women who had had a third pregnancy. Only tests taken according to these criteria were counted as items of service which were eligible for reimbursement for the general practitioners taking the smear. Many health authorities operated their own recall schemes which became superimposed upon this national pattern, and the arrangements for the centralised recall scheme have now been withdrawn (DHSS, 1981). Each health authority is expected to make its own arrangements for call and recall of women for screening.

Within this rather vague outline, it is perhaps not surprising that the actual service delivered has varied considerably between different areas; in addition, the nature of service delivered bears little relationship to a regular five yearly examination of women over 35.

A review of routine statistics generated by the pathology laboratories participating in cervical cytology testing, and by the NHS Central Register was presented by Roberts (1982). There has been a rise in the annual number of examinations carried out from about 7×10^5 in 1965 to 2.9 million in 1980. Most of this increase has resulted from smears taken by general practitioners (see Table II.9). The age-breakdown of the examinees is also shown - it is notable that only a minority of smears are taken from women aged 35 and over. Information on the results of smears is notified to DHSS on forms completed by pathology laboratories and hence a 'detection rate' (positive cases per 1000 total smears) can be estimated. Table II.10 shows estimated numbers of tests and the detection rate by age and place of testing for 1980.

Statistics derived from forms HMR 101/5 are likely to underestimate the amount of cytological testing performed, since a proportion of smears are not accompanied by this form. Special studies are required to obtain a complete picture of activity, and to elucidate the nature of the population being tested in more detail. The study in Yorkshire in 1976-77 (Parkin et al, 1981) had this purpose in mind (Table II.11). It was found that approximately one third of tests were from various hospital sources, mainly from gynaecology departments, or tests taken in association with pregnancy (an estimated 80% of women having a child are tested before or soon after delivery). One third of the women reported 'symptoms' at the time the smear was taken, although more common in gynaecology patients it was not confined to this group. The separation of smears into 'routine tests' and 'diagnostic tests' is certainly not clear-cut on the basis of place of examination. In any case the notion of a 'diagnostic' smear is a curious one; most of the pathological conditions sought by cytology ('cervical intra-epithelial neoplasia') are asymptomatic, and a pap-smear is certainly not an appropriate investigation if symptomatic carcinoma is entertained as a diagnosis. The taking of smears from symptomatic subjects is probably better considered as an example of selective screening; such women have a higher rate of abnormal cytology than asymptomatic subjects (see below) which probably reflects common risk factors for various gynaecological diseases. Attendance in relation to age and marital status is shown in Table II.12. The overall average attendance rate of 10.6% is the percentage of women aged 15 or more living in the study area having a test in one calendar year. Within this overall rate are larger variations by age and marital status. Between 20% & 25% of married women aged 20-39 attended in one year, but attendance rates fall off with age, and are lower for single women and widows/-

divorcees than for married women. In order to achieve five-yearly testing of the population, the minimum attendance rate must be 20% per annum - however this supposes that no repeat tests are carried out, which was far from being the case; 17.5% of the examinations were repeats of tests on the same person during the 2 years of the study. Attendance was clearly related to social class; there was a higher than expected proportion of attenders in social classes I and II than in IV and V.

The screening programme in Manchester has been described in a number of publications (Sansom et al, 1970, 1971) as far as testing of 'asymptomatic women" - i.e. excluding hospital tests - are concerned. As in the Yorkshire study, the majority of tests were on women aged less than 35, and social classes IV and V are underrepresented in women receiving tests. The results of a planned policy of recall for repeat tests after 3 months, 1 year, 2 years and 3 years has also been evaluated (Sansom et al, 1975).

In addition to the DHSS policy described above, two other series of recommendations have been formulated for England and Wales.

(1) The British Society for Clinical Cytology published a series of recommendations in 1977 (Spriggs & Husain, 1977).

i) Age for beginning screening : 25 for women presenting for contraception, pregnancy or venereal disease; 30 if sexually active and not already tested.

ii) Intervals of five years over age 35 (or three yearly if resources permit). A first smear in a woman aged over 35 should be followed by a second smear within a year to guard against false-negative smear.

iii) Screening should cease at age 70 (but no age limit for first test).

(2) A working party was set up by the DHSS Committee on Gynaecological Cytology in 1980 to consider possible changes in the current policy on age and frequency of screening. This was largely a response to increased mortality rates and the increasing numbers of positive smears in younger women. The recommendations of this committee have been published (Draper, 1982). They are summarised below.

i) Smears should be taken at ages 35,40,45,50,55,60 and 65.

ii) No further smears need be taken for women aged over 65 who have had

at least two recent negative smears (e.g. ages 60 and 65) and who have never had a positive or doubtful smear.

iii) A smear should be taken early in the course of each pregnancy.

iv) A smear should be taken at age 22, or next visit thereafter, for women attending for family planning advice, and who have not previously been screened.

v) A smear at age 30, for women attending for family planning advice, and who have not had a test during the previous five years.

vi) A smear should be taken on one occasion (or perhaps two) from any other woman aged 25-35 who is, or has been, sexually active and who requests a test.

vii) Smears taken at gynaecological clinics and STD clinics are considered useful (but two smears during the same diagnostic process are considered inappropriate).

3.2.2.2 Screening programmes elsewhere

ABERDEEN

A screening programme, originaly aimed at married women aged 25-60, was started in Aberdeen in 1960, personal invitations to attend being sent by post (McGregor et al, 1971; McGregor, 1976). Rescreening on a five-yearly basis has subsequently been continued and smears are also taken at family planning sessions and during pregnancy. It is claimed that by 1969 almost 90% of women aged 25-60 had been screened at least once. McGregor and Teper (1978) compared mortality rates for the Grampian region (including Aberdeen) and Tayside, with those for the rest of Scotland where, it was stated, there is no established screening programme. Death rates in the screened areas appear to be lower than in the unscreened (although the significance - if any - of the differences is not reported).

CANADA

The 'Walton Report', published in 1976, reviewed in part II available data for the Canadian provinces in terms of the intensity of screening (number of cytologic examinations as a percentage of the female population), the proportion of tests which were first examinations and

the outcome in terms of change in incidence and mortality rates. The recommendations made by this report were that screening for women 'at risk' (i.e. sexually active) should be :

i) An initial smear at age 18.
ii) If initial smear satisfactory and negative, a second smear after about one year (to allow for false negative examinations at first screening).
iii) If initial smears negative, three yearly tests to age 35, then five yearly to age 60. If all tests have been negative, screening should then cease.

In addition, it was suggested that annual screening should be undertaken for a high risk subgroup, defined as women with early onset of sexual activity and multiple male partners. To this end cytologic specimens were to be taken at family planning clinics, student health clinics, youth clinics, venereal disease clinics, prenatal clinics and at medical facilities where women are examined before admission to penal institutions.

These recommendations have been reviewed and revised in a further report of the Canadian Task Force (1982). It seems that the task force considered most women born after 1945 to belong to the previously defined 'high risk' subgroup (and expanded this subgroup to include women whose husbands or sexual partners had had multiple partners). Accordingly the recommendations were changed, the concept of a 'high risk' group abandoned, and annual screening recommended for all women between the ages of 18 and 35 who have had sexual intercourse. After the age of 35, five yearly screening is suggested (although women over 35 considered as high risk, by themselves or their physicians, are not to be discouraged from having smears more frequently). These recommendations are based in part upon results of a computer simulation exercise undertaken by Yu et al (1982) - see Section III.

FINLAND

The screening programme in Finland was introduced in the early 1960's. Every woman receives a personal invitation to be screened starting at age 30 or 35 and then at five year intervals until age 55. Response rates to invitation for screening are over 90% (Hakama & Rasanen-Virtanen, 1976). This programme which is run by the Finnish Cancer Society accounts for less than one third of the smears taken in Finland (Timonen et al, 1974).

The effect of screening on incidence of cervical cancer in Finland and the other Nordic countries has been evaluated by Hakama (1982) - see Section 3.2.3.

ICELAND

Screening started in 1964, and from 1969 onward the policy is to examine women aged 25-70 at intervals of 2-3 years (Johanneson, 1978). There appears to have been a favourable impact on incidence on mortality rates.

NORWAY

In Norway, an organised screening programme was introduced in Ostfold county in 1959. This took the form of invitations to attend for screenings (intervals 2,3 and 3 years) for women aged 25-59. The programme yielded information on attendance rates for screening, and rates of onset of clinical cancer in women who did or did not attend. No generalised routine screening programme has been introduced in Norway.

EAST GERMANY

In 1973 programmes were set up in Berlin and Rostock to study the effect of different organisations (Ebeling et al, 1981). In Rostock personal invitations were sent via a computerised system, whilst in Berlin cytological examination was carried out during routine gynaecological examinations with no personalised invitation. In both cities the objective was to screen all women aged 20-65 every 2 years. It seems that the degree of coverage achieved was about the same for the two systems. A fall in incidence of clinical cancer, most notably in the age-group 40-59, has been observed.

USA

For many years the general recommendation in the USA was to screen at annual intervals after the age of 18 years. Recently a consensus statement was issued by a group convened by the NIH (NIH, 1980) which recommended: -

i) Virgins should not be screened for cervix cancer.
ii) Screening should begin 'soon after the onset of sexual activity'.
iii) The first smear should be repeated after an interval of one year.
iv) Rescreening should be carried out at intervals of 1-3 years (the

precise figure to be decided jointly by the woman and her medical care provider).

v) No further screening if two negative smears are obtained after age 60.

There have been several studies from the US reporting the results of screening programmes, usually in terms of changes in incidence and mortality rates. However, it is often very difficult to identify the precise nature of screening carried out.

In Toledo (Burns et al, 1968) an attempt was made to invite all women over 30 for examination once per year by their own physicians - participation was well below this target, but a decrease in invasive cancer was clearly observed.

In Louisville (Kentucky) a programme was instituted in 1956 which attempted to examine all females over the age of 20, and by 1967 it was estimated that over 90% of the population had been examined at least once. A decrease in mortality rates for Jefferson county (including Louisville) was contrasted with the absence of change in the rest of the state where, it is presumed, less screening was carried out (Christopherson et al, 1970).

In Olmsted County (Minnesota), it was estimated that up to 63% of the female population were examined at least once between 1960 and 1967 and the average number of tests per woman was 2.7 (though there was no organised programme as such). A fall in invasive cancer incidence and mortality were observed for the same period (Dickinson et al, 1972a).

3.2.3 Evaluation of screening

Ideally the value of screening for carcinoma of cervix should be demonstrated by a controlled trial, comparing incidence of clinical cancer in the screened group with the unscreened. No such trial has ever been mounted, so that the evidence available is less direct.

It is clear that women who do not attend screening programmes have much higher rates of invasive disease and are detected at later stages than those who do (Fidler et al, 1968; McGregor, 1976). However, women who do not attend screening programmes are very frequently those at higher risk of disease, and disease rates in the unscreened population are found to be higher than those seen before the introduction of screening (Hakama & Rasanen-Virtanen, 1976).

This self-selection bias makes interpretation of results in screened vs non-screened difficult and unconvincing.

Cross-sectional studies attempt to relate the intensity of screening in different areas with incidence or mortality of cervical cancer. The study of Hill (1975) suggested that in countries where a decline in mortality rates was probable, almost all had implemented screening programmes (this paper is frequently cited as evidence of a universal decline of mortality rates prior to screening, but in fact does not show this). Within the United States Cramer (1974) found a positive correlation between the decline in mortality rates and the annual rate of screening in each of the states. Miller et al (1976) related an index of screening intensity (smears/1000 women/year) with changes in mortality from uterine cancer for Canadian provinces and for counties or census subdivisions. The results suggest that greater levels of screening are associated with larger declines in mortality, even when various socio-demographic variables for the geographic units are controlled for.

Guzick (1978) has reviewed the many studies which report trends in incidence or mortality from cervix cancer in relation to the introduction of screening programmes. For almost all centres, incidence has declined since the introduction of screening (it was usually steady, or rising, beforehand), and mortality rates also decline, usually some years later than fall in incidence. Tables II.13 and II.14 are reproduced from this review.

Undoubtedly the best analysis of this kind is that reported by Hakama (1982) who presents incidence data from the Nordic countries in relation to screening. In these countries cervical cancer incidence was slowly rising during the 1950's and 1960's. Nationwide screening programmes were introduced in Finland and Iceland in the 1960's (all eligible women received personal invitations) and the majority of women had been screened within a few years of their introduction. In Sweden the programme was introduced more gradually (county by county), in Denmark only some counties have been covered by organised mass screening, whilst in Norway the only organised mass screening has been in Ostfold county. The effect of screening on the trends on cancer incidence are clearly seen in Figure 2.16. Within those countries showing the clearest changes, the age-groups subjected to screening (30-59) show a fall in incidence which is not apparent in the older age-groups (Fig 2.17). A much clearer effect is seen when the cohort curves for each country are examined. In Norway there is a progressive rise in incidence at all ages for successive birth cohorts (up to 1948). In Finland, Sweden and Denmark, however, the

cohort curves for those generations subjected to screening appear to be lower than expected in relation to earlier generations.

Similar changes are seen in the cohort curves for cancer incidence in England and Wales (Parkin et al, 1984). Until the 1921 cohort the curves appear regular and parallel, there is then an abrupt fall in the 1926-1936 cohorts, after which the rates again begin to show a rise (Fig 2.18). Using data on registrations of in-situ cancers, an attempt was made in this paper to estimate how much of the change seen is due to changing risk of disease in the different generations, and how much is the result of screening. The curves in Fig 2.19 represent the incidence rates as they would have been, assuming no screening, and that half of the detected in-situ cancers would have progressed to clinical cancer, the mean lead time being 8 years (several different distributions of lead times in the detected cases were tested, but made little overall difference to the pattern observed). The cohort curves in this figure are much more plausible in terms of changes between the succeeding generations; they are more clearly parallel, and show a maximum incidence at about 50-55 years. They are rather similar to the pattern observed in Norway, which, as already stated, has had little organised mass screening whereas the curves actually observed (Fig 2.18) show changes similar, though less marked, to those in Finland, Sweden and Denmark. Using this simple model of probable events in the absence of screening, Parkin et al (1984) estimated the reduction of incidence attributable to screening in England and Wales (Table II.15).

A rather different approach to evaluation of the effectiveness of screening is to utilise the methodology of the case-control study to estimate the protective effect of screening tests. The principles involved have been discussed by Morrison (1982). Clarke and Anderson (1979) investigated the screening histories of 212 cases of cervix cancer and 1060 age-matched neighbourhood controls. The outcome measure was the degree of protection conferred by a screening test in the five years preceding the year of diagnosis - unscreened women had a relative risk of 2.7 compared to those screened. A recent study in Geneva (Raymond et al, 1983) tends to confirm these findings - the protection conferred by one or more negative tests up to 10 years before diagnosis (or the finding of a positive smear) was estimated to be 3.2.

3.2.4 Problems to be solved

It seems quite clear from the numerous studies cited in the preceding section that cervical cytology screening has been effective in reducing incidence and mortality from invasive cancer. The main problem remains,

however, the decision on the nature of service to implement. Section 3.2.2 has outlined the very great variety of policies that have been suggested or implemented. They are defined in terms of ages for testing, frequency or intervals between tests, adjustment of protocols to allow for high risk groups and the organisational setting for tests. Essentially the choice of programme involves a decision on how the maximum benefit from screening (defined as invasive cancers avoided, or life-years saved, perhaps) can be obtained from a given input of resources. This is a decision based on analysis of cost vs. effectiveness. (In the wider context of health care planning, the decision must be made as to the appropriate resources to devote to screening for cervix cancer as opposed to a totally different health programme; this need not concern us here). The value of a screening programme is likely to vary considerably depending on the precise pattern of service delivery adopted. For this reason the simple checklist approach to deciding the value of screening - for example the well known criteria of Wilson and Junger (1968), over-simplifies the issue by dichotomising the decision (screening useful/not useful). The simultaneous evaluation of many different variables on a quantitative basis requires some form of modelling approach. This is considered in section III, but it is useful here to briefly review the factors which have to be considered in the practical planning of a screening service.

Screening of the population always involves selection of subgroups for examination. In the context of cervical cancer screening these are usually defined in terms of age-groups (and, of course, sex!). The choice of age-groups for screening depends, logically, upon a knowledge of the natural history of disease. At the very least the prevalence of the condition sought by the screening test in different age-groups should be known. In practice, since screening will not be a single event, but a process repeated at intervals during the life of an individual, knowledge of natural history should include age-specific incidence rates of the conditions sought, and their duration, and how this varies with age. The review of natural history in II.2.3 has indicated the lack of detailed knowledge in this area.

As well as age, screening policies may use other risk factors to define groups suitable for selective screening. It has already been noted that the variables associated with an increased risk of clinical cancer are associated also with higher risk of dysplasia and carcinoma in-situ. The variables used as criteria for defining different policies do not have to be directly causative. From a practical point of view this is of little consequence beside the requirement that the relative subgroups can be easily identified. It should be noted that selective screening need not imply an 'all or none'

policy - screening only a particular subgroup of the population. Indeed, as far as cervical carcinoma is concerned none of the known risk factors which could reasonably be used have a high enough relative risk, or are sufficiently prevalent, to justify screening only a subset of the population (Hakama et al, 1979), but it is easy to envisage policies which include the more frequent screening of certain subgroups. Several demographic variables are associated with increased disease risk (e.g. social class/occupation, marital status, parity), as is current contraceptive practice. Hammond et al (1968) found that women with 'complaints' (e.g. spotting, bleeding or vaginal discharge) were at 2-3 fold risk of cervical cancer (invasive or in-situ) for more than ten years after two consecutive negative smears. This is in accordance with the increased prevalence and incidence rates of precursor lesions in symptomatic women (section II.2.2) and such women form an obvious category for more intensive surveillance.

As well as being related to disease risk, it is clear that there are a number of individual factors which are associated with attendance at screening programmes, marital status and social class, for example, (Parkin et al, 1981). These are both, as already described, associated with risk of disease. Several studies suggest that non-attenders at screening programmes are a particularly high risk group, having incidence rates which are higher than those expected on the basis of incidence observed before the introduction of screening (Hakama & Rasanen-Virtanen, 1976; Boyes et al, 1981). This is not entirely surprising since non-attenders would be likely to be less health conscious and more exposed to risk factors for cancer of the cervix. Thus, the probability of attending for screening examinations is not equally distributed in the population, attendance for future examinations can be to some extent predicted from past screening history. These are important to consider when predicting the outcome of a screening service, and in the practical planning of service delivery.

Much of the literature on cervical screening concentrates on describing the mass-screening programmes which have been added onto the health care system. In reality, as described, a considerable amount of testing goes on independently of such programmes - in gynaecology departments, V.D. clinics or associated with pregnancy, for example. Although in the planning or evaluation of screening projects it is convenient to ignore such tests (they are often dismissed as 'diagnostic' investigations) they may form a substantial proportion of the total examinations carried out. The women examined in these settings frequently have higher rates of abnormality than the self-selected group who attend screening clinics. Such testing probably has a substantial

effect on the natural history of the disease in the community, and furthermore, tests taken at the time of other health-care activities represent only a marginal increase to the cost of the encounter. An examination at a screening clinic solely devoted to asymptomatic testing is likely to be more expensive. For these reasons the existence of 'incidental' testing should be taken into consideration when screening programmes are being planned (the latest recommendations for England and Wales (Draper et al, 1982) appear to go some way towards this).

The effects of lack of validity in the screening test itself have been discussed in 3.2.1. The improvement of sensitivity and specificity of the smear depend upon adequate technique in the taking and examination of the specimen, essentially questions of quality control. It is worth noting that the published data on false positives and predictive values usually come from academic centres, and laboratories with interested and motivated staff. The reality in a service setting may be lower sensitivity and specificity than commonly reported. In addition to this, an area that has been little discussed is the efficiency of follow-up and treatment when an abnormality has been identified. Policies here appear to vary considerably; in general, coloscopy and biopsy (perhaps preceded by a repeat smear) may be recommended for severe cytological abnormality, minor dysplastic changes may be followed by a series of smears repeated at intervals. It is unlikely that such follow up is perfect, patients are likely to be untraced or unwilling to return. Kinlen & Spriggs (1978) were able to report the outcome in 101 women with severe (grade IV-V) cytological abnormalities who escaped follow-up for at least two years, and the drop-out rate for minor abnormalities is likely to be much greater. Even after treatment by cone-biopsy recurrence of abnormal epithelium has been reported (Kirkup et al, 1979), although this probably represents inadequate treatment of the initial lesion.

The design of screening programmes should also take into account secular trends in disease risk. It has been discussed in section II that in England and Wales there appear to be quite marked changes in the risk of cervix cancer (and presumably of its precursors) according to birth cohort. Screening programmes should probably consider therefore whether intensity of examination should change over time.

III SIMULATION MODELS

1. DEFINITIONS

A model is merely a well-defined, well organised picture or description of some aspect of the real world in which we are interested. This is indeed the meaning of the word in everyday usage, and, although models may be qualitative in character, scientific study usually requires the use of mathematical models with a large quantitative component.

Four functions of models are commonly defined (Last 1982).

Predictive models are used to estimate the expected outcomes from one or another response to a situation - for example population projections based on different assumptions about fertility.

Organising functions of models include the synthesis of a complex of related factors into coherent forms. In order to handle these complexities, the variables used in the model must be conceived in a way that makes them accessible to quantification, qualification and manipulation.

The mediating function reveals common ground between formulations that appear distinct or disparate at first sight, but where the disparity is the result of a narrow or individualistic viewpoint.

The analysing (or explanatory) function involves models that pose different choices among the possible relations between variables. These are models in which the same manifestations or results are obtained as the result of different causal sequences. These different pathways demonstrate where future studies are likely to be profitable in obtaining information on the most likely causal pathway.

Early applications of mathematical models in the health care field were concerned with modelling infectious disease processes, and the relatively simple relationships involved often allowed these to be expressed in mathematical terms (Bailey, 1975). Ideally, the expression of relationships into an exact formula leads to the identification of a mathematical solution. However more realistic and complicated models lead to extremely difficult mathematical problems which may prove intractable or uneconomic to solve. The advent of the computer has meant that there is less need to obtain elegant mathematical solutions, and simulation techniques are much more easily

applied. The objective of a simulation model is quite different from the analytical model, which sets out to summarise a set of observed relationships as a concise algebraic equation and identify a generalisable solution. Simulation is used to express the process rather than summarise the result, and comparisons between the outcome of the process and available observations are used to validate the adequacy of the model.

Many simulation models in health sciences work on the principle of the Markov chain, which requires specification of a series of defined states, and a set of transitions between them. A 'deterministic' model is one in which the results or model output can be predicted directly from the input, and the transfers carried out are proportional to the number of units in the initial state. For example, if we have 100 units in A and a transfer rate from A to B or 0.5, exactly 50 units will be transferred.

A 'Stochastic' model is one in which a probability element is incorporated into mathematical formulae. In the example above, transfer of units from A to B would be a random process, with the probability that any particular individual will transfer being 0.5. The model output is expressed in the form of a probability (or probability distribution), so that, for example, the number of individuals in a particular state lies in a given range with a particular probability.

An intermediate type of model (the 'Monte Carlo' model) uses probability to generate the effect of chance or randomness on the situation being described by using a deterministic model structure and allowing the chance factors to influence, for example, the magnitude of transfer rates for individual units. The difference between this type of model and a fully stochastic model is that the latter is able to produce generalisable solutions and give confidence ranges as an output, which Monte Carlo models can only do by running the model a number of times.

2. THE USES OF MODELS IN STUDIES OF SCREENING

Simulation models have many advantages in exploring the outcome of complex processes. At the very least they force the investigator to clearly identify and quantify the premises from which he is working (which was termed the 'organising function' above).A simulation model of a screening programme will therefore require precise, quantitative statements about natural history of

the disease and the screening test characteristics. The relative importance of the various premises to the outcome of the simulation can readily be explored, a process termed 'sensitivity analysis'. Some assumptions about the disease or the process of screening which might seem a priori of great importance may be found to be irrelevant to the outcome. The challenge that the simulation is not realistic because of the false premises used (for example, about rates of attendance for screening) is readily met by performing a simulation with alternative assumptions. It may be that some of the values needed for the model may only be present as possible ranges, or orders of magnitude. A range of outcomes can be produced in order to express the effects of such uncertainty - in effect producing a 'confidence interval' in addition to point estimates.

Another advantage of the modelling approach is that it allows the checking of model assumptions against observed data - the numerical values of the parameters used - for example incidence of disease, prevalence at different ages etc. should be consistent with those observed. Simulations using real data should produce results which seem consistent with those observed in screening programmes. In fact, the construction of a simulation model involves the use of data on observed phenomena to help explain the processes involved in the natural history of disease (a 'positivist' approach), as well as the use of various assumptions about the natural history and the screening process to predict possible outcomes (a 'structuralist' approach).

The construction of a computer simulation model has an added advantage in that programming is generally done in one or other high-level computer language. The advantage of these is their structured, unambiguous format which requires that all the relationships modelled must be explicit and quantifiable.

The major objective underlying the use of mathematical and computer simulation models of screening programmes has been to serve a predictive purpose. They have primarily been developed to answer questions concerning the outcome of screening populations following the implementation of different screening policies. Traditionally, of course, this is the role of the controlled trial. It is, however, now probably impossible to carry out trials of screening in real populations, both for ethical and technical reasons. Although there is theoretically no ethical dilemma, in that the effectiveness of screening is still controversial, in reality any such trial proposed would be deemed unacceptable. The technical problems in designing a realistic trial are also formidable. The large number of variables which require consideration (eg ages and frequency of screening characteristics of target populations)

would make such trials impossibly large (or numerous) and lengthy. It is quite likely that after a large number of such trials, a high proportion of research workers and clinicians would remain unconvinced of the results because of differences in the populations of women, the manner of screening, type of treatments etc. Doing a large number of trials carries with it the increased risk of two similar trials showing different results by chance - leading to calls for further trials. 'Artificial' experiments using simulation are eminently practicable, however, and have the advantages already alluded to, of being repeatable with different assumptions or incorporating new data, for example on improved screening techniques or treatment for clinical disease.

The value of the modelling approach was stated succintly by Neuhauser in a minority report to an 'NIH Consensus Statement' on cervical cancer screening (NIH 1980). The Statement consists of suggested policies for screening, which is presumably based on the collective guesses of the experts gathered together at NIH in July, 1980.

The minority report concludes : "Computer-based models should be widely available in interactive form allowing providers and patients to vary the assumptions and consider the results. These models should be used in high school courses and in health science museums. On the surface the controversial issue is the frequency of screening. The real issue, however, is the role of computer models in clinical decision making. These powerful techniques are new to medicine, and not enough doctors are being educated in their use. This pap smear debate will be viewed as one of the historical landmarks in this transformation in clinical reasoning".

The analytic function of such models has been less extensively explored. For carcinoma of the cervix, as will be discussed, there is considerable debate about the precise natural history of the disease process. Dunn (1953) was the first to extensively analyse in a quantitative fashion the type of information that could be gathered from screening, and now this might be used to define parameters in the natural history. The approach was taken further by Knox (1966) who estimated sample size and follow up period required in order to clarify the simple parameters of prevalence and incidence of preclinical disease, and sensitivity of the screening test.

3. REVIEW OF PREVIOUS WORK

An early use of mathematical modelling to study cervical cytology screening was that of Dickinson & colleagues (Dickinson et al 1972, Dickinson 1972). They used life table survival analysis on groups of patients found to have cervical cancer (including stage 0) before and after the introduction of screening, and applied an equation formulated by Berkson & Gage (1952) to estimate cure rate and mortality risks in the two groups. The increased expectation of life in the patients detected when screening was in progress was used to evaluate the costs and benefits of screening during this period.

Eddy & Schwartz (1982) refer to this type of modelling as a 'Surface Model' - it is used to tabulate observations and estimate the consequences of an existing screening program. There is no attempt made to describe the underlying disease process, or the dynamics of screening which led to the observed events. "Deep Models" incorporate knowledge or assumptions on such parameters, and are hence able to examine potential outcome of a variety of possible policies which might be implemented. The other models reviewed are all of this type.

The earliest work was that of Knox (1973, 1976) who developed a generalisable computer simulation model for examining the outcome of screening policies. The model was deterministic in type, and simulates events occuring in a cohort of 10,000 women as they age from 15 to 95, the size of the cohort being decremented each year of simulation in accordance with the expected number of deaths, (mortality rates were obtained from a current life table). The natural history of the disease is simulated by specifying up to 26 pathological "states" (including normal, dead of this disease, dead of other causes) between which the population is divided. Up to 50 different types of transition are allowed between these different states, the rate of transition being expressed as the proportion of individuals who move from one state to the other during each year of the simulation. A degree of sophistication is introduced by making these transfer rates dependant upon age (for transfers from the normal state) OR on duration in the starting state (for other transitions).

The screening process is simulated by a series of specifications: the pathological states to which screening is to be applied, the probability that an abnormality will be detected, and the state to which the proportion found 'positive' will be transferred. Note that the sensitivity of the screening

test is thus required to be quantified for each abnormal state specified in the model, since it is the proportion in each such state that are detected by the test. The specificity of the screening test is in fact entered as false positive rate (1-specificity), ie the proportion of normals who are found to be positive and transferred out of the normal state.

The final series of specifications for the model Knox calls 'resource deployment', and are the ages at which screening is to be "offered" to the cohort (up to 30 individual ages) and the percentage of the population who "accept". The uptake of screening programmes real life varies according to factors such as age, marital status, social class etc. (Sansom et al, 1970, 1971; Parkin et al, 1981). Knox's model addresses this by making uptake of screening dependent upon state (reasoning that the risk factors for cervical cancer, and its precursor conditions, are the same as those that determine attendance rates, or acceptance of screening).

Knox used the model firstly to explore the range of different natural histories that were compatible with observed local data on cervical cancer incidence and the prevalence of preclinical conditions (actually the prevalence data for carcinoma in situ observed in British Columbia (Fidler et al, 1968) and incidence of clinical cancer in Birmingham were used). A range of possible options were found to be feasible, and, two broad categories of natural history; 'progressive' and 'dynamic' (the latter allowing for regression of carcinoma in situ to normal), used for exploring screening options. Various criteria are possible for evaluating outcome of screening programmes, these include the percentage of deaths averted (compared to background, no screening situation), the number of tests carried out per averted death, and the number of positive tests per averted death. When a programme of screening involving few tests per lifetime was simulated, he found that these outcome measures were not very sensitive to the different assumptions about natural history, but this became much more critical when between five and ten screenings were carried out per lifetime. The marginal returns of screening - that is the number of tests needed for each extra death saved - became progressively smaller with increasing investment in screening. Decisions about the apparent optimum ages for ten tests per lifetime were sensitive to the choice of outcome measure; lives saved, life years saved, or life years weighted in favour of the young.

Knox's work has recently been repeated by a group in Canada (Yu Shun-Zhang et al, 1982) who used the identical computer program. Some simplifying assumptions were made : for example only one preclinical pathological state

(carcinoma in situ or worse) was modelled, and the possibility of detection, surveillance and intervention before this ignored. The natural history incorporated into the model was based initially on incidence data of carcinoma in situ (or worse) in British Columbia (Boyes et al, 1982). However these rates were tripled and the maximum incidence advanced five years to allow for "an earlier and possibly more rapidly progressive natural history than that ... in the cohort born in 1929-33". In addition, onsets of preinvasive disease were limited to ages under 55. Rates of progression to clinical cancer, regression and mortality were adjusted to produce incidence and mortality rates of invasive disease consistent with this hypothesis but it is not clear whether such rates are compatible with observed data, nor whether model predictions of prevalence of in situ disease are compatible with those actually observed in British Columbia. The results are presented in terms of ages at which the cohort should be screened in order to produce different potential years of life saved, given different levels of input (number of tests), test sensitivity and attendance.

Coppleson and Brown (1975, 1976) describe the development and use of a simulation model similar to that of Knox. Only four states (normal, dysplasia, carcinoma in situ and invasive cancer) are used with a series of transition rates between them. The basic data chosen for their model were prevalence data of dysplasia and carcinoma in situ (Bibbo et al, 1971) and incidence data of clinical cancer from the Third National Cancer Survey in the US (Cutler & Young, 1975). They found that a range of possible transition rates were consistent with these data, but that it was necessary to postulate transition rates dependent upon age (hence implying that the sojourn times are related to age, duration in state, or both). The preferred set of transition rates which they chose to examine screening options incorporated the maximum possible rate of regression from dysplasia to normal, and the minimum possible rates of transfer out of the state of carcinoma in situ.

They studied the outcome of different screening policies (specified as different ages for screening) using cancers avoided, life years saved and weighted life years as measures. The optimum ages for screening were dependent upon the outcome criteria chosen (although the relationship between total tests per lifetime and percent of the maximum possible saving achieved was not). They also examined the effect of different false negative error rates (1-sensitivity of test) on the percentage of possible savings that can be achieved by a given number of tests per lifetime, and the marginal costs (further tests needed) of finding each case according to the number of screenings already done with different false negative error rates. Finally,

they undertook a simple cost-effectiveness exercise by imputing a dollar cost to each test and examining the theoretical financial consequences of different outcomes for a stationary population. Unlike the analyses of Knox, no correction is made for differential compliance with screening, and no attempt was made to study the effects of other assumptions about natural history.

The Knox model has been adapted and used by a group of workers in the Netherlands (Habbema et al, 1979). They first attempted to overcome one of the major defects of the model, that it allows only for the testing of a single birth cohort at different ages, by performing eight separate runs on different birth cohorts. This allows a more realistic prediction of results in the Dutch population where screening policies introduced in a given year will be available for different lengths of time for separate cohorts. The group have produced some results of sensitivity analyses where the possible effects of Dutch screening policies are examined in terms of incidence and mortality of invasive cancer given different assumptions about natural history (duration and possibility of regression of carcinoma in situ) and test sensitivity.

A later publication by the same group (Oortmarssen et al, 1981) describes the development of a different approach which aims to overcome some of the other drawbacks of the single cohort deterministic type of model. A model using a micro-level Monte Carlo simulation is described, in which the individual lifehistories of a single birth cohort are simulated. For each individual the age at death (from a life table) is determined, and also the age at hysterectomy (from a probability table, source unspecified). The onset of disease and transfers between the states of disease declared as the natural history is a stochastic process which depends upon sets of transition probabilities and dwelling time distributions for the different states. These parameters are derived more or less empirically, and several theoretical natural histories developed. Onto this background simulation of natural history can be superimposed screening for disease, and this can be either "routine" screening (eg at gynaecological attendance), or as part of a mass screening policy. The latter is simulated by specifying ages at test offer, acceptance rates, detection rates (test characteristics) and the outcome for individuals detected as positive. A wide variety of options is available for treating this latter category.

Model output is essentially a comparison of various parameters in the whole cohort between the background conditions (what would happen to each individual if no intervention had taken place), and the outcome for the same

individuals in the presence of screening. The indices used include disease cases saved, lives saved, life-years saved, number of false-positives etc.

The advantage of this micro-simulation approach is that it permits the modelling of interactions between factors; for example age-specific prognosis distributions, correlations between sojourn times in successive disease states, the non-independance of attendance probabilities at subsequent screens, and between test errors on subsequent screens. The model also addresses the possibility of having different risk strata in the population, and permitting the evaluation of different mass screening programmes against a background of "routine" testing.

However the basic philosophy of the single cohort approach is essential for this model - a knowledge of what would have happened to each individual if they had not died, had a hysterectomy, or been found positive on screening. The difficulties in this approach were highlighted in these workers' earlier paper, specifically in validating simulation results against those observed in a population with changing disease patterns in different cohorts. Although not explicitly stated, there must also be problems in defining realistic transitional probabilities for hysterectomy and attendance at routine screening, since the only available data are likely to be cross sectional, and cover short periods of time.

Albert et al (1978 a,b) describe a mathematical model for examining screening programmes. Its main objective appears to be analytical, attempting to define the natural history of cancer as a series of mathematical functions, rather than relying on the specification of states in a Markovian process, with transfer rates between them. Thus the natural history of cervix cancer is described as the distribution of sojourn times in the preclinical state (which, incidentally is assumed to be exponential, with a mean of 7-8 years and independant of age). The model examines the outcome in a population of women with an age distribution of the US 1960 population over a fifteen year period.

The outcome measures used relate to the proportion of disease detected in in-situ or micro-invasive states as compared to later stages, in the presence or absence of screening; the model is unable to examine effects on mortality. The effect of a policy of annual screening is tested, and compared with highly theoretical policies based on formulae which provide the optimum distribution of tests at different ages to secure maximum benefit for minimum investment. The authors claim no more than to have produced an initial methodology for the

examination of screening programmes in general. Some of the assumptions required in order to supply inputs for the model appear highly questionable, and no attempt to examine the sensitivity of the results to different assumptions has been made.

In a highly technical and detailed monograph, Eddy (1980) describes the formulation of a theory which is stated to be generalisable to the solution of all screening problems. The specific discussion is limited to analysis of screening for cancer of the breast, however. It seems that his model has been applied to cervical cancer screening, since a diagram linking increased life expectancy and cost is reproduced; however no detail is available.

IV THE IARC SCREENING MODEL

1. CONSTRUCTION OF THE MODEL

1.1. Introduction

The development of the simulation model currently used was a progressive process, the original starting point being the computer program written by Professor E.G. Knox some 10 years ago. A brief description of this macro-simulation approach has already been given (section III), and two developments of this are currently being used.

a) A conversion to an interactive menu-driven format. This program (MACRO) has been used for teaching and demonstration purposes. Its simple output and ready adaptability allows demonstration of the effects of frequency of testing, ages of testing, acceptance of screening and test sensitivity with different assumptions about natural history.

b) A simplified version (GENMAK) has been used to explore possible natural histories. The main simulation model utilises sets of transition rates between states ; some of these are available from published data (eg incidence of dysplasia, mortality from clinical cancer), others can be derived as possibilities compatible with observed incidence and prevalence of disease.

The Knox model, in studying transfers between states every year in a single cohort, cannot distinguish between the variables of age and time. In the natural history of the disease, for example, the rates of onset, progression or regression of pathological conditions can be made dependant upon age, or (with more difficulty) on duration of disease, but not upon both. This is a major drawback. It is most obvious in any attempt to simulate survival of clinical cancer. Survival curves (adjusted for normal mortality) are strongly dependant upon the age at diagnosis. However within each age-group survival probability also depends on duration since diagnosis; hence the curves of relative survival are not simply exponential, but show a steep fall in year one, and then progressively flatten out. This variation by age and duration may also be important at other points in the natural history; the probability that different progression rates pertain at different ages has already been described.

It is, in fact, a general property of the Markov process that probability of transfer from a state is independent of the time already spent on it. One way to circumvent this is to define the states in the simulation as a combination of pathological entity and duration. In one version of GENMAK the programme GMTO this approach has been used, so that up to 2100 states are used - as an array of 21 (pathological conditions) X 100 (durations). Transfer rates are declared for any combination of these 2100 states. This solution becomes impracticable if it is wished to make events in the simulation depend upon several other variables.

The incidence of preclinical and clinical cervical neoplasia have been shown to be related, albeit indirectly, to a variety of variables which include age, parity, marital status, social status, contraceptive use. Some or all of these may be of value in specifiying screening programs. In order to incorporate these into a macro-simulation model the technical problems involve the use of transfer specifications between the elements of multi-dimensional arrays. Although such problems are theoretically soluble, the second drawback of macro-simulation - inability to make events dependant upon past history - is not.

Past history or experience of individuals is important for example in attempting to simulate screening programs. The macro-simulation model mimicks screening by defining ages at which screening tests will be offered, and specifying the percentage of the population at these ages that will accept. If some of the population are not screened (ie are "refusers") they will not receive another "offer" until the next specified age, at which time the acceptance rate will be again the same as that for the general population. In reality both these premises are highly unlikely ; persons not receiving a test at the specified time are likely to receive further invitations during the interval before the next routine examination is due, and individuals who do not accept screening are likely to comprise a subset of the population with a greater than average probability of refusing subsequent offers also.

Another major disadvantage of the simulation models described in section III is their limitation to the examination of events in a single birth cohort. The results of such an exercise are interesting, but will be far removed from observing the results of screening programs in real populations which are composed, of course, of all generations. The simulation of screening involves the 'offering' of testing to the cohort at defined ages, however in reality screening policies are likely to be introduced (or modified) at a single date or point in time, and hence affect the varying cohorts of the population in

different ways. In addition there is good evidence of a strong birth-cohort effect on the natural history of cervical cancer in England and Wales and the Nordic countries.

Another element that is important to incorporate into a model of screening programs is 'incidental screening' - for example in relation to family planning, childbirth, hospitalisation. Although this is often conveniently ignored, it often makes up a large proportion of the examinations performed (Parkin et al, 1981). It is hard to conceive how this type of activity could be simulated in parallel with routine screening programs using the macro-simulation approach.

For all the above reasons the fundamentally different approach of microsimulation was chosen as the basis for the current model. The general outline of this approach is described below, followed by more detailed description of the varying elements of the simulation with the specifications of the data and the sources used. Technical details of the computer programs are contained in section IV.2.

1.2. General Format of the Model

The model studies events occurring in a population of women over a defined period of time. The time period chosen is arbitrary but in all the examples below a 30 year period has been studied in order to avoid projections too far into the future when there are obviously likely to be many uncertainties. The population studied is one with realistic demographic characteristics; once again the choice is arbitrary, all the work described below has been carried out on a population that has the demographic makeup of that of England and Wales.

Like the Knox model, the simulation involves examining year by year transitions occurring between defined, mutually exclusive states. These include various more or less arbitrary steps in the natural history of disease (including death from cancer), as well as states of normality and death from other causes. However, instead of examining the proportions of a group which transfer each year, the IARC model studies transitions occurring to individual members of the population. Each individual has a set of characteristics pertinent to the study of screening. As already suggested in the preceding

section it was desired to make transfers between states dependent upon a variety of factors other than age :

- Duration in the current state
- Marital status
- Childbearing
- Past history of screening

Offers of screening and their acceptance by individuals in the population can also be dependent upon these factors.

Each individual in the population is characterised by their values for a set of variables related to these characteristics. There is no theoretical limit to the number of variables which may be defined for each individual ; however since the model will involve examining each individual every year, the addition of variables will add to the time and computing load involved.

The following represent the variables in a relatively simple version :

DEMOGRAPHIC VARIABLES

1. Age : As year of life, ie 31 = age 30 last birthday
2. Marital status : Single, married or formerly married
3. Parity : Nil, one birth, two or more births
4. Fertility status : Fertile/infertile

NATURAL HISTORY

1. Present state : Disease state, includes normal/dead
2. Duration in present state
3. Previous state

SCREENING HISTORY

1. Clock : Years to elapse before next screening due

The basis of the model is the annual examination of individuals to determine whether the value of these variables change. The simplest change is the Age variable, this will be incremented by one every year providing the individual survives each year. The probability of dying can be obtained from a life table, and is, of course, conditional upon age. Thus the basic data which

is used by the model consist of conditional probabilities ; in this example the probability of death given age and current state (the probability will, of course, be greater for subjects with cancer).

The other main feature of this model is that it is stochastic in nature, the events which occur are determined by chance within the probabilities defined. For instance, using the mortality example it might be that the data specifies the probability of dying for a woman aged 60 during the ensuing year as 1 %. How is the occurrence or non-occurrence of death to be simulated ? The model uses a random number generator which would produce a random digit betweeen 1 and 1000 ; if the digit produced was 10 or less, the person in question would be deemed to have died, and the value of the relevant variable changed accordingly. If she survives she would be eligible for other transitions within the model, and of course the value of the age variable would be incremented by 1.

This approach has intuitive appeal in that it is very close to reality in the way it treats individuals as units, rather than carrying out operations on fractions of populations. However it suffers from a drawback of real life too: the use of random chance in the model means that no two simulation runs will ever be exactly identical even with the same data as input. The results will, in fact, obey the laws of probability, and conventional inferential statistics are required to decide whether the differences observed between different simulation runs are in fact real, or merely due to chance. For the same reasons, simulation exercises involving large populations are likely to result in more precision in the results (ie narrow confidence limits) than those involving small samples.

There are additional advantages in a model which results in the recording of events in individual members of the population, one is the ability to use the model for retrospective analyses. As described in the introduction, the case-control approach to the study of screening is likely to be increasingly used in future. The output from the stochastic model, consisting as it does of individuals with defined characteristics, can be utilised for simulating case-control studies. This is a further check on the validity of the model and the assumptions which it incorporates.

1.3. Simulation of Demographic Events

As already described, the model aims to simulate events in a population with the demographic characteristics of that of England and Wales. The

starting point for the simulation is 1961 when complete data on this population was available from the census.

The first stage in a simulation run is to choose a size of population to be studied. Two considerations govern this choice. Firstly the microsimulation model is expensive in computer time, and, because each individual must be examined for her characteristics before a decision on transfer is taken, the amount of processing time needed is proportional to the size of the starting population. The second consideration is related to the fact that, because the model works on individuals, the outcomes of simulation runs are like real life experiments; no two outcomes on the same size of population will be identical. Consequently, the size of population simulated should be large enough to obtain reliable results.

Once the population size is fixed, it is distributed by age, marital status and parity to match the England and Wales 1961 distributions. Table (IV.1) shows the age distribution used - each individual is assigned an age in accordance with this distribution. The next step is to distribute the population by marital status. Table (IV.1) also shows the distribution of marital states at each individual year of age for the 1961 England and Wales population. The actual procedure involves examining each member of the population in turn, and allocating a marital status according to the probabilities pertaining to the relevant age, the actual decision being left to chance.

The third step of the 'start up procedure' involves distributing the starting population by parity. Questions on the parity of married and formerly married females were included in the 1961 and 1971 censuses, and tabulations of the data are available. However there is no comparable information on parity of single (never married) females by age. Some data are available on trends in illegimate births (Werner, 1982) and a question on parity was included in the General Household Survey for 1979 (See Table IV.2). These allow some 'guestimates' of parity of single women, which are included in Table IV.3. The procedure for allocating parity status to individuals involves, once again, random chance within the probabilities defined for the relevant age and marital status.

The demographic events which can occur in this population over the 30 years of the simulation are births, marriages and deaths. The procedure involves examination of every individual for each year, and a decision is taken whether or not a change in status occurs. Once again this is done by

comparing a randomly generated number against a set of conditional probabilities.

Step one is a decision on survival. The appropriate probabilities are life table death rates (P death| age). For the first 20 year period the life-table death rates for England and Wales for 1970-72 are used (Table IV.4). The second step is to stimulate transitions between marital states. Three marital states are used ; single, married and formerly married (widowed or divorced) and three transitions are possible between these states (marriages, remarriages, divorces/widowhoods). The transition probabilities were obtained from age-specific rates of marriage, remarriage, divorce and widowhood for two separate periods, 1961-1970 (Table IV.5) and 1971-1980 (Table IV.6). Two sets of data are used because of changing patterns of nuptiality. Inspection of the tables reveals a rather later age of marriage in the second decade, and of course, rising rates of divorce leading to increased rates of transition from married to formerly married in the younger age groups. The latter parts of the simulation (1981 onwards) involve projections of rates. The full data for the model involves the use of transition rates for individual years of age; these have been estimated by linear interpolation and the full data set (FILE 14.DAT) is shown in Appendix 5 and as Table IV.7.

The third demographic event to be simulated is fertility. An attempt has been made to define age-marital state-parity specific fertility rates. Fertility rates in the population are notoriously subject to short term fluctuations, and the British population has shown quite marked and rapid changes in the last two decades. Ideally a set of fertility data appropriate for each individual year of simulation could be incorporated; however this would lead to an inordinately cumbersome set of data files, and a compromise of adopting average rates for the decades 1961-70, 1971-80, 1981-90 has been adopted. As will be seen in the Results section, this leads to some slight deviations in the simulated population structure from that observed, but these are small and do not affect the main objective of the model, that is to study the effects of screening.

Table IV.8 and IV.9 show the data used to calculate age-parity specific fertility rates for 1961-70 and 1971-80 for married women, and the results obtained. Fertility data for unmarried females is not broken down into single vs. formerly married, nor is it possible to produce estimates by parity of mother. The model therefore has to utilise the data for the two decades as shown in Table IV.10, and assume equal rates for single and formerly married, and at all parities. The full data set used by the model utilises rates for

single years of age. These were obtained by graphical interpolation in similar fashion to the calculations of Tables IV.9 and IV.10. The full data is shown in FILE 13.DATA, in Appendix 5.

It is worth noting that the data for marital and parity transitions are presented as central rates (r) of fertility, marriage etc. These are converted to transition probabilities (p) before being used in the model by the formula

$$P = \frac{2\ r}{2 + r}$$

The actual occurrence of a birth to an individual depends, once again, upon comparison of a randomly generated number against the appropriate age-marital state - parity specific probabilities.

The births which result are used to define new entrants to the population as infants in their first year of life (Age = 1). Since the population being simulated consists only of females, the proportion of births which are girls requires to be known, and is shown for different maternal parities in Table IV.8 and IV.9.

In practice the application of childbearing probabilities to the entire population leads to a progressive deviation of the parity distribution from that expected on the basis of real or projected demographic data. With increasing years of simulation the proportions approximate to a Poisson distribution, with a deficit of para 0 women. This was overcome by specifying a proportion (P_i) of the starting population and new births deemed to be infertile. A reasonable estimate of this proportion is 0.05 (WHO, 1975). An adjustment is required during the start up procedure to ensure that all infertile individuals are placed in the Para 0 category. In addition, an appropriate adjustment must be made to the chilbearing probabilities for Para 0 women, since the probability of childbearing is only applicable to fertile women.

1.4 Hysterectomy

From the viewpoint of the simulation model a further event of great significance in a woman's life history is a hysterectomy (for conditions other than cancer of the cervix), since she is then no longer at risk of this disease. The rate of operation for hysterectomy has shown a steady increase in the last two decades, so that prevalence of hysterectomy is rising, and there are also marked cohort efforts.

In order to calculate rates of hysterectomy, data was obtained from the Hospital In-Patient Enquiry (HIPE) which collects information on 10% of all hospital discharges in England and Wales. The number of hysterectomies involving removal of the cervix which were performed in 1966 and 1976 for conditions other than malignant neoplasms of the cervix uteri were calculated for each five year age group (see table IV.11). Somewhat similar data, for different time periods, had been used by Alderson & Donnan (1978), and by extrapolating their hysterectomy rates backwards in time they were able to estimate the prevalence of hysterectomy at different time periods. Table IV.12 shows prevalence of hysterectomy by age in 1961 as presented in their paper. Similar estimates of prevalence by age for 1966 and 1976 have been used to correct the denominator populations in Table IV.11, so that the final hysterectomy rates calculated are actually probabilities of hysterectomy in women who still have a uterus. The sets of rates for 1966 and 1976 are used to approximate hysterectomy rates for the decades 1961-70 and 1971-80 respectively.

Hysterectomy is handled by the model as one of the 'States of Disease' (see below), since it clearly excludes the possibility of any other stage in the natural history being present in the individual. Transfers can occur from normality, or from preclinical stages of cervical cancer (but not clinical disease). The model allows for transfer probabilities from preclinical carcinoma of cervix to hysterectomy to be multiples of the basic rate (from normality), in accordance with the possibility that preclinical cancer and other conditions which necessitate hysterectomy share common risk factors. It is also possible to specify transition probabilities dependent on parity and marital status. However, the data to permit this do not exist so the data used in FILE 15 DAT (see Appendix 5) uses a single age-specific set of hysterectomy rates.

Individuals who have had a hysterectomy no longer participate in childbearing.

1.5 Simulation of the Disease Process

The disease process is simulated by defining a series of mutually exclusive 'states' in which an individual is situated at any particular moment. The natural history of the disease is mimicked by postulating transitions between these states, the rates of which are conditional upon other characteristics of the individual.

After defining the size of population to be simulated, the second specification required is the number of states involved in the simulation. These must include a 'Normal' state, and states to represent dead (of causes other than cervix cancer), and hysterectomy (for other than clinical cancer of cervix), as described above. Other states are used to define the disease process, and the possible transfers between these states are then included in the data files.

The simplest natural history, and the transitions involved between the states used to define it is shown in Fig. 4.1. Although there are obvious advantages in specifying the simplest natural history possible - a minimal number of transfer probabilities require to be defined for one thing - unfortunately the resultant model is a poor reflection of reality. Preclinical disease exists in a variety of grades of severity from the presence of minimal cellular changes to occult invasive cancer, and these different grades have different probabilities of detection on screening, and are treated and followed up in different ways.

As already discussed in section II.2 preinvasive neoplasia can be regarded as a single condition 'Cervical Intra-Epithelial Neoplasia' of varying grades of severity. However this terminology is relatively new, and most of the literature on natural history of cervix cancer still uses the terms 'dysplasia' and 'carcinoma in situ'. Despite the dichotomisation of what is clearly a continuum of pathological change, this old terminology does have an advantage in a simulation model. It allows the 'dysplasia' category to include histological patterns which may or may not be precursors of cervical cancer. The transient nature of much of what is detected as 'dysplastic change' can be modelled, whilst the workload involved in diagnosing and following up such cases is recorded.

The states which have been used in the examples below, and the possible transitions between them, are shown in Fig. 4.2.

1.5.1 Prevalence of disease states in the starting population

The first step in simulating natural history, once the disease states have been defined, is to define the prevalence of each in the population at the beginning of simulation (1961). Clearly this does not apply to the two 'dead' states, and the data used for defining prevalence of hysterectomy has already been defined above.

1.5.1.1 Prevalence of preclinical disease is available from a variety of series describing the results of screening programmes. Prevalence rates of dysplasia and carcinoma in situ for several such series are shown in Figs 2.7 and 2.8. It should be recalled that the prevalence rates presented are actually based on the prevalence of true-positive screenings, and the true prevalence rate can be derived by dividing by the sensitivity of the screening test.

A set of age-specific prevalence rates for the preclinical states dysplasia (2), carcinoma in situ (3) and occult invasive cancer (4) are shown in Table IV.13.

1.5.1.2 Prevalence of clinical cancer Table IV.13 also shows prevalence rates for clinical cancer. By "prevalent cases of carcinoma of cervix" is meant women currently alive who have been diagnosed as having carcinoma of cervix at sometime in the past. This data is not available, and a reasonable estimate must be produced.

The approach used was to use the simple deterministic model GENMAK (see Appendix 1). The data input were age-specific incidence rates of clinical cancer of cervix for England and Wales from a period before the widespread introduction of screening, and estimates of age-duration-specific survival data for the same period. Suitable incidence data are shown in Table IV.14. Age-specific survival data for carcinoma of cervix in England and Wales are available for cases registered in 1971-1973 (see 1.5.2. below), and estimates of survival rates around 1960 can be made from crude (all ages) survival curves from this period. The simulation output is the number of cases in each of the declared states, from this the prevalence of cases of cervix cancer, by age, can readily be derived, and these are given as 5 year age-specific rates in Table IV.13.

The population to be simulated by the model is made up of individuals with a variety of defined demographic characteristics (age, parity and marital state). So far prevalence has been presented as if it were dependant only upon age. However it is known that prevalence of preclinical conditions is independently associated with other variables and data on age-standardised prevalence ratios for parity and marital status are available (Parkin et al, 1982 a ; Sweetnam et al, 1981). The data used in calculating starting prevalence are shown in Table IV.15. It was not possible to use the data of Sweetnam et al, which provides prevalence ratios for dysplasia, c.i.s. and invasive cancer separately, since it was available only for ever-married

females, however the ratios for married : formerly married in their data (Fig 2.9) are close to those in Table IV.15. The prevalence ratios shown in the table were thus applied to all states of disease (dysplasia, cis, microinvasive, clinical cancer). The ratios presented were simply multiplied to provide nine parity marital status specific prevalence ratios (although this is probably not accurate, there is no alternative approach possible due to limitations of data).

A special program (CRESTPREV - See Appendix 2) takes the 5-year age specific prevalence data, the parity-marital status specific prevalence ratios and, using the age-parity-marital status composition of the starting population as weights, produces a full set of starting prevalence data in FILE4.DAT (Appendix 5).

The model once again uses a random number generator to determine an individuals starting state, given the probabilities of the different states conditioned upon age, marital status and parity.

1.5.2 Derivation of transition rates between disease states

It has already been pointed out that the choice of disease states for use in the model is an arbitrary one. The more states defined, the easier it becomes to model disease and screening processes ; for example Knox (1973) defines 26 different states. However the more states that are used, the more difficult it becomes to determine realistic rates of transfer between them. Although a major virtue of the use of simulation models is the ability to explore a variety of assumptions about input parameters, it is also true that the major criticism is the lack of realistic data that can be incorporated. Hence it is advisable to try to define disease states such that reasonable estimates of their prevalence and the rates of progression and regression between them can be obtained.

Fig. 4.2 represents the choice of disease states used in the examples described. The data used to derive rates of hysterectomy and mortality from causes other than cervical cancer have already been outlined.

One other set of transition rates are known with a fair degree of certainty, those from clinical cancer to death from carcinoma of cervix. Such rates are equivalent to relative survival rates from clinical cancer, rates for England and Wales are shown in Fig. 4.3. It should be noted that survival curves such as these do not show a constant rate of decline - ie the

probability of death is not constant each year. The risk of death is highest in the first year after diagnosis and declines thereafter. Such curves can only be modelled by specifying rates which are dependent upon duration in the starting state.

It has been suggested that other rates of transition may be dependent upon the duration of the state or disease condition (see section II.2).

It should be remembered that what is being modelled is an essentially continuous process; the extension of cellular abnormalities to involve the entire thickness of the cervical epithelium and subsequent invasion, and progressively increasing cellular atypia. When this is simulated by a set of discrete 'states', it seems unlikely that the transition between them would be entirely independent of the duration of abnormality. Certainly there is no reason to suppose that the distribution of sojourn times in such preclinical stages of disease can be simply modelled by rates of ingress and egress depending solely upon age. A constant rate of exit from a state would lead to the distribution of sojourn times following a negative exponential; to date there is no evidence for or against such a distribution, but it seems intuitively less likely than, say, a log-normal distribution. For these reasons the model allows transition rates to be dependent both upon age and upon duration in the initial state.

Data derived from the survival curves of Fig. 4.3 are included in the transition data shown in Tables IV.16-IV.18.

Two other sets of data can be used directly to approximate transition rates, these are the incidence rate of dysplasia and the incidence of clinical cancer. Dysplasia incidence can be used to approximate the transition rate from normality to dysplasia. Estimates of incidence of dysplasia have been presented in II.2.3 ; such figures are derived from serial observations on groups of women attending screening programmes. As already discussed, the figures represent incidence of true positive tests, and the true incidence of dysplasia can be estimated by dividing by the sensitivity of the screening test; this is probably about 70-80% (see section II.3.2).

The incidence of dysplasia which is estimated thus from observation of serially screened populations will represent the net increase of dysplastic cervices resulting from conversions from, and regressions to normality. The true annual transition rate from normality to dysplasia will thus be higher than the observed incidence depending on the rate of regression (dysplasia to

normal) and the actual intervals between screenings on which the estimates of incidence were based. Neither of these are known, so the transition rates cannot be estimated precisely. The rates shown in Tables IV.16-IV.18 are approximations based on the two lower curves of Fig 2.10.

The other observed data which can be used to estimate transition rates are the incidence rates of clinical cancer. These indicate the annual number of cases passing from the preclinical states (in Fig. 4.2 this is always micro-invasive or occult invasive disease) to clinical disease. Clinical cancer incidence figures for populations of England and Wales prior to the introduction of screening programmes are shown in Table IV.14.

The use of the data on incidence of dysplasia and clinical cancer, along with prevalence of preclinical disease and clinical cancer (see section 1.5.1 above) to derive sets of transition rates, is illustrated in Appendix 3.

1.6 Simulation of Screening

The descriptions of screening programmes in section II have indicated that in reality these are really rather complex. Recommendations are usually formulated in terms of ages and frequencies for examination of asymptomatic women ; for example the age recommended for the first examination, the intervals between subsequent tests, and the age after which screening can be ceased. These recommendations are based upon a mixture of intuition, qualitative judgement, some results of quantitative modelling, and political pressures. However, such recommendations usually assume that no screening activity exists apart from the programme envisaged. This is far from true - large numbers of smears are taken at a variety of contacts with the health care system. These cannot be ignored as incidental or unconsequential, since the women examined may be particularly high risk groups (using contraception, having gynaecological symptoms) such tests form an important part of the preventive strategy for carcinoma of the cervix.

Since the micro-simulation model follows individual subjects, it is possible to simulate contacts with the health care system and the screening which can arise on such occasions. The easiest of these is the screening activity which occurs in ante-natal and post-natal clinics. Since the model simulates childbirth events to each individual, it is very simple to incorporate the performance of a screening test during a childbirth year. Data on individual frequency of other events is more difficult to incorporate, but it is theoretically possible to model contacts with family planning services and

inpatient or outpatient visits to gynaecology and veneral disease departments. Screening can occur at all or a designated proportion of such contacts.

Routine asymptomatic screening is simulated by defining the programme which is offered to individuals, their acceptance of the offer, and the characteristics of the screening test. The data for defining a programme is included in the model as FILE12. DAT. The screening programme can be made up of many different policies. Each policy is contained in 3 lines of data which define:

i) The years for which the policy will be in operation
ii) The interval between offers of screening tests
iii) The ages between which tests will be offered
iv) The marital-state of individuals to be offered screening
v) The parity " " "
vi) The percentage of women in each disease state who attend for screening when it is offered
vii) The proportion in each disease state who are found to be positive on screening, and moved to state "STPOS"
viii) The proportion in each disease state, who have been found to be positive on screening and placed in STPOS, who revert to original state the following year

It will be recalled that each individual has a set of associated variables which include age, marital state, parity, current state, previous state and duration since last screening (ICLOCK). The probability of attendance when screening is offered can be made dependent upon age, marital status and parity (by specifying separate policies) or upon current disease state. The sensitivity and specificity of the screening test is modelled by defining the proportion in each disease state who are found to be positive, and moved to state STPOS, when screening is performed on those who attend. The proportion in state 1 (normal) found to be positive is the false positive rate (1-specificity), the proportion in the disease states (dysplasia, cis, micro/occult invasive) found positive on screening is the sensitivity of the test for these conditions. Data on test characteristics have been given in section II.3.2.

When the screening test is found to be positive, the individual's current state becomes STPOS and a record of what the previous state had been before screening is naturally retained as the variable LSTAT. The fate of women in this 'screened positive' state will naturally depend on their previous state.

It is assumed that, in reality, some form of investigation of positive screenees is undertaken depending on the severity of the cytological changes observed. Naturally women who were false positive will not undergo any prolonged observation or treatment, this is modelled by returning all of these individuals to state 1 (normal) the following year. Women with marked cytologic changes will undergo investigation by, for example, colposcopy and biopsy, and the histologic changes appropriately treated. Such women can be retained indefinetely in state STPOS ; in this case they take no further part in the natural history of cancer, nor in screening, and can leave STPOS only by having a hysterectomy or by dying from causes other than cancer. Finally, women detected by screening may escape supervision, possibly because follow-up was arranged by a recommendation for repeat smears which is not complied with, or biopsy may be refused. In such cases the individuals return from STPOS to their original disease state. The percentage of women with pathological lesions detected by screening who escape supervision is modelled by specifiying a percentage of STPOS women reverting to their original state each year (see line 3 of the policy data in FILE12.DAT). It is possible to modify the model so that this probability depends on the time since the positive screening test.

Women who attend for screening are not due for a further test until the interval specified in the screening policy has elapsed. This is simulated by the variable ICLOCK, which after a screening test has been carried out is set to this interval. ICLOCK is decremented by 1 each subsequent year. Only when the value of ICLOCK is zero is a woman eligible for screening. The variable ICLOCK can be used to simulate 'refusers' of a screening programme; for example the value can be set to other than zero for women who do not attend the first offer of screening.

The model output records the total number of screening tests performed each year, the number of false positives found, and the number of true positives for each disease state.

2. THE COMPUTER PROGRAMS

2.1 The main simulation program and input data files

The computer program is written in FORTRAN and is structured with liberal comments to explain the sequence of operations that is being carried out. The

program is reproduced in its entirety in Appendix 4, and the data files used in Appendix 5.

This section will briefly outline the principles and structure of the program as a guide to understanding.

The MAIN LOGIC SECTION defines the variables used and the size of the arrays. A call is made to FILE 33.DAT which defines one of the outputs (FOR034). This output will contain a count of the numbers of individuals defined by any of combination of variables (age, marital state, parity, state etc) at any of the 30 years of the simulation. FILE 33.DAT is shown in Appendix 5 and the output from this specification appears as FOR034 in Appendix 6. Calls are made once to five subroutines which define the starting population at the beginning of simulation (INIT, ST AGE, STMST, ST IPS, and ST IST). For each year of the simulation, three other subroutines are called : TRANSF, SCREEN and AGEING.

Subroutine INIT reads in the data in FILE1.DAT which includes the number of years for which simulation is to be carried out, the size of the starting population and the total number of states (NUMST). When this total number is defined, the following states can be allocated a number :

STOTH	(dead of causes other than cancer)	= NUMST
STHIS	(dead of cancer of the cervix)	= NUMST - 1
STHYST	(hysterectomy - not for cancer)	= NUMST - 2
STPOS	(screening test positive)	= NUMST - 3

In addition, the years for which a file containing the data on all the individuals in the simulation is to be saved is recorded.

Subroutine ST AGE takes the starting population and distributes it according to age, using probabilities derived from the population structure in FILE1.DAT.

Subroutine ST MST takes the starting population and for each member allocates a marital status with regard to age, the probabilities of marital state conditional upon age are derived from FILE2.DAT.

Subroutine ST IPS takes the starting population and for each member allocates a parity status, with regard to age and marital state. The relevant probabilities are derived from FILE3.DAT.

It will be remembered that, since the model is stochastic in nature, the application of probability tables involves separate decisions for each individual. This is achieved by calls to a subroutine RAND (I,J) which produces a random integer I in the range 1 to J. This integer can be compared with the number relevant to the individual from the probability table.

Subroutine ST IST allocates one of the states defined in INIT to the starting population. The probability of each of the live abnormal states (ie state 2 to STHYST (NUMST-2) is determined by combining the data on prevalence of hysterectomy in the starting population (FILE1.DAT) with that on the prevalence of clinical cervical cancer and its precursors (FILE4.DAT). The latter defines disease state probabilities in terms of age, marital status and parity. The duration in state has next to be allocated for those states (1-5) from which exit is possible. For state 1 duration is made equal to age. For dysplasia (2) and cis (3) the durations are allocated from files FILE92 and FILE93 respectively. These represent cumulative probabilities of each duration for individual year of age, and were derived during the formulation of transition rate data as described in Appendix 3. For state 4, duration is either 1 or 2 (with equal probability). The duration in state 5 (clinical cancer) has been derived from the survival curve (all ages), which for the purposes of simulation will be sufficiently accurate, and is simpler than the use of a data file containing separate estimates for each year of age.

Once this initialisation procedure is complete the starting population is completely defined in terms of age, marital status, parity, state and duration in state, values for these variables being assigned to each individual.

The simulation proper now begins with calls to three subroutines for each year of the simulation run.

TRANSF.: This subroutine carries out all the transitions between states on a year by year basis. For each decade of the simulation (Year 1, 11 or 21), the transfer data contained in FILE11.DAT is read. Each individual in the population is then examined to see if they transfer to a different state. There is the opportunity to undergo a second transfer in the same year; however, the probability of doing so is halved (since, on average, the first transfer would have occurred at mid year, and only a half year remains for the second). The probability of subsequent transfers is progressively reduced by dividing by two. As soon as a transfer takes place, the variables for current state (IST), last state (LSTAT) and time in present state (ITIMM) are updated - the latter variable taking the value 0. A further set of transfers is

possible - from STPOS (screened positive) back to the original state pre-screening (LSTAT). These probabilities are defined in the screening data file (FILE12.DAT). These transfers out of state STPOS are the first event simulated each year (except for the first year, at the beginning of which no one has been screened, and there are no individuals in STPOS).

SCREEN: This subroutine performs the simulation of routine screening. The data defining the screening programme is read from FILE12.DAT, which contains a series of policies, each of 3 lines of data. These policies may be relevant only during certain years of the simulation run. If screening is to be done during a given year, each individual is examined to see if they are eligible for screening, given their age, marital and parity status, current disease state and time since the last test was performed. Once an individual has had a routine test, they are not deemed eligible for the next until the time interval defined by the screening policy has elapsed ; this is achieved by means of the variable ICLOCK.

If an individual is eligible for screening, a random number is generated to see if she attended (the probability of attending given the current state is defined in the data file). If the individual attends another random digit determines whether she is found to be positive (the probability of which depends upon current state, and is defined in the data file). If found to be positive the variable present state (IST) takes the value STPOS, and LSTAT, ITIMM and ICLOCK are changed appropriately. ICLOCK is decremented by 1 each succeeding year - when it takes the value of 0 the individual is eligible for screening once again.

Non-attenders at screening can be dealt with in various ways - either recalled for screening after a specified interval, or not offered a further test until the next examination is due. This is done by adjusting ICLOCK.

An annual and running total is kept of the number of screening tests carried out, and the number of non-attenders.

AGEING: This subroutine carries out all the vital events - births, marriages and deaths - each year, as well as ageing the individuals in the population. The data which are used are the probabilities of childbirth (in FILE13.DAT), of changing marital state (in FILE14.DAT) and of death from causes other than cancer (in FILE15.DAT). The latter file also has data on the probability of having a hysterectomy. For each individual the actual occurrence of such events is simulated by the generation of a random number for comparison

against the probability relevant to the individual, given their age, marital state, and parity.

The sequence of demographic events simulated is : -

1. Marital events
2. Births (unless infertile, or in STHYST (hysterectomy))
3. Hysterectomy
4. Deaths (from causes other than cervix cancer)
5. Ageing by one year of survivors

Each year the value of ICLOCK (time before next routine smear is due) is decreased by 1 and the value of ITIMM (time in current state) is increased by 1.

Infants (aged 0-14) are handled rather differently, since none of the demographic events except death, are relevant to them. Every year the number of infants in each age group is checked to see if any deaths occur (using the mortality data in FILE15.DAT), if not they are moved up to the next age group. Infants moving from age 14 to age 15 become adults, and are examined as such the following year. The births that occurred earlier in the subroutine are checked to see if they are female (the relevant probabilities depend on birth number : 0.483 (first), 0.485 (second), 0.488 (third)). Female births become infants aged 0, and are added to the simulation population.

2.2 Output files

During a simulation run, the main program generates 4 types of output.

Channel 6 is the default output channel. When the model is run in real time at a terminal this can appear on the screen, or it can be assigned, as it is when the simulation run is in batch, to a file.

For each year of the simulation output to channel 6 consists of a matrix showing the transitions which occur between the defined states during the year, and the number in each state at the end of the year. In addition, the number of births occurring and the number of screening tests performed during the year is recorded, together with the total population alive at the year end. A running total of screening tests is also kept, both as the total number performed and the number of 'positive' tests. It should be noted that the number in state STOTH (ie dead from causes other than cancer) is not

accumulated from year to year, this figure represents the annual deaths only, whereas STHIS (dead from cancer) cumulates the total cancer deaths as the simulation goes along. At the very beginning of a simulation run, data for "Year 0" appears, representing the results of the start up subroutine ST IST and showing the distribution of the population among the different states before any transfers take place. An example of the output from a typical simulation run is shown in Appendix 6.

In addition to this regular output, a cross-tabulation of numbers of individuals by any combination of variables can be obtained at the end of any particular year. This is done by specifying the years for which such files are to be created in FILE 33.DAT and the variables, intervals etc required. For each of these years, the data is read out to channel 34, into files which become sequentially numbered.

The examples given show numbers of individuals by age-group and disease state.

Three further output files are created which will allow the computation of parameters of interest.

FOR008 lists deaths from cancer amongst the population.

FOR009 lists new cases of cervix cancer.

For both these files the variables for each individual is recorded as one line of data, with year of simulation.

FOR010 is a block of data recording for each year of simulation the number of person-years of life lived at each age.

2.3 Programs for analysis of ouput

The output described in FOR008, FOR009 and FOR010 is processed by a program RATABLES (Appendix 7). This produces tables of incidence and mortality rates by five and ten year age-groups for the time periods specified in the data-block of the program.

In addition, a calculation is made of the person-years of life lost at each year of simulation. This is carried out using the age of cases dying (in FOR008) and a data block containing the normal expectation of life at each age

(from the 1970-72 life table). The person-years lost are cumulated for each year of simulation.

The output of RATABLES is printed as FOR020, an example of which is reproduced in Appendix 7.

V RESULTS OF SIMULATION

The format of the output generated by the simulation programmes is illustrated in Appendix 6. In this section the data generated has been summarised in tabular or graphical form, rather than reproducing multiple examples of computer output.

The results will be reviewed under three headings; firstly the results of simulation of demographic events, secondly the results of simulation of cervical cancer natural history, and thirdly the results of simulation of different screening programmes.

1. SIMULATION OF DEMOGRAPHIC EVENTS

The objective of the screening model is to investigate the effects of different screening policies in a realistic population over relatively short time periods. The population chosen was one having an identical composition to that of England and Wales in 1961 (the census year) and simulation is possible for a 30 year period. For the first 20 years of this period, input data for the simulation of vital events have been taken from the observed rates in England and Wales, for the third decade published estimates have been used (see section IV). The objective of the simulation is to keep the structure of the model population close to that observed, or predicted for England and Wales. A precise concordance is not expected, since the modelling methods are rather coarse - involving for example ten-year average (rather than annual) rates and taking no account of migration.

Table V.1 shows the changes in population size observed (and projected) for England and Wales in the period 1961-1991 and the results of simulation (average of several runs using data shown in Appendix 5). Table V.2 shows the crude birth rates and death rates (females only) for England and Wales in comparison with the simulated rates (from R20.LOG, Appendix 6). There is a reasonable correspondence, except for a deficit of births at the beginning of the second decade of simulation, and a slow rise in mortality (which in practice appears to have remained rather constant). The latter effect may be due to the use of a single life-table for the entire simulation period (whereas expectation of life has in practice shown a slow increase over time). It does not seem to be the result of inaccurate modelling of the population age-structure. The model results are compared with the observed England and Wales population pyramids in Figure 5.1.

Fig 5.2 shows the observed and simulated age-specific marital composition of the population. The main change with time is a shrinkage of the proportion of never-married women, and an increase in size, especially at young ages (25-55) of the formerly married group. The model predictions closely match the changes observed over the period 1961-1981.

Fig 5.3 shows the proportions of married females of different parities. Once again the model predictions are a reasonable approach to the observed data. The results of the 1981 census are not available, and an estimate based on the General Household Surveys of 1980-1982 is shown against the model output for 1981.

2. SIMULATION OF DISEASE OCCURRENCE

Although not part of the disease process, the simulation includes the modelling of hysterectomy (for conditions other than carcinoma of cervix and its precursors), since this will have an effect on the occurrence of disease by changing the susceptible population.

Fig 5.4 shows the prevalence of hysterectomy, by age, at four different time periods of a simulation run of 30 years. The model suggests quite a marked rise in the prevalence of this condition, given the rates of hysterectomy in the input data of FILE15.DAT. These prevalences are compatible with those estimated independently from similar data sources (Table V.3).

Figs 5.5 and 5.6 illustrate the age-specific prevalence of dysplasia (state 2) and carcinoma in situ (state 3) at 4 different times in the course of simulation. Two different natural histories are used. In both the transition rates are those shown in Table IV.16, but in 11M the incidence of dysplasia is made conditional upon age, marital status and parity (as described in Appendix 3), whilst in 11A, incidence is dependent upon age alone. With 11A there is relatively little change in the prevalence of preclinical disease over time. However with 11M there is an increase in prevalence of both conditions with time. As already described, this reflects the changes in (especially) marital status of the population, and reproduces to some extent the underlying secular trends in disease rates.

Fig 5.7 shows the observed age-specific incidence rates of carcinoma of cervix in England and Wales, for the period 1962-1965 (i.e. before the introduction of screening could have markedly influenced the incidence). The age-specific incidence rates for the first five years of a simulation are

shown for comparison. The close concordance of the two curves is not surprising, since the natural histories used by the model were developed so that the observed incidence rates were reproduced as closely as possible (Appendix 3). After this initial time period there is, however, a progressive divergence between the results of simulation and the observed rates of incidence and mortality (Fig 5.8). This is to be expected, since the England and Wales rates shown are the net result of complex changes in risk of disease by birth cohort and the effect of screening in preventing clinical cancer (Parkin et al, 1985). The predicted rates shown are the results of simulation using the two natural histories 11A and 11M referred to above. The result of changes in marital/parity composition of the population on simulated prevalence of preclinical states has already been described; here the end result on incidence and mortality can be seen as a rising trend with history 11M (where incidence of dysplasia is conditional upon these two variables) and almost constant incidence and mortality when history 11A is used. Neither of these simulations incorporate any screening activity, and so represent the theoretical background of disease occurrence onto which screening will be superimposed.

3. SIMULATION OF SCREENING

The number of combinations of natural histories, screening policies, attendance rates, test characteristics etc which can be specified and examined, is of course enormous, and in this section only a limited number of these possibilities are presented. An additional problem is the determination of which outcome parameters are of interest - the output from the model provides a great amount of information on the simulated population, and this must be summarised for ease of comparison.

The approach adopted below is to have available several simulation runs in the absence of any screening activity, so that the average values of the outcome parameters can be calculated. This solution has been used because the model is stochastic in nature, and the results of simulation runs vary somewhat, even though the input variables remain constant. The results obtained when different screening policies are incorporated into the simulation are then compared with this baseline. Three outcome parameters have been examined in the examples which follow: the reduction in the number of new cases of cancer, the reduction in the number of deaths from cervix cancer, and the reduction in life-years lost due to cancer. These three parameters do not necessarily change to similar degrees - much will depend, for example, upon the age at which screening is concentrated. The relationships are complex

(which is why a simulation model is necessary for their study), but in general screening at younger ages that prevents incident cases of clinical cancer might save more life-years than a policy with an equal detection rate concentrated at later ages. These savings resulting from screening are presented as absolute values (cases saved, lives saved, life-years saved) and as percentage reductions from the baseline no-screening results. This allows a direct comparison of the effects achieved on the different outcomes.

In health care studies life-years are not uncommonly used as outcome measures, and the further refinement of calculating weighted life-years is sometimes performed. This procedure gives more value to life-years saved at younger ages than in the elderly, the logic being that social costs of death in the young are greater than in the elderly. Although this approach may have something to commend it, it is difficult to decide on an appropriate weighting to use (personal judgement of what is appropriate may depend on the age of the person making it!), and it has not been adopted here.

In comparing screening policies it is not sufficient merely to examine the outcome in terms of the savings defined above. These must be compared with the input of the screening programme (otherwise the 'optimum' programme in any comparison is likely to be the one with the most intensive screening). The costs of a programme are likely to be reflected by the actual number of tests carried out, and by the work involved in the further examination and treatment of individuals found "positive" at the screening test. In the analysis presented below, therefore, programme input is given as total tests performed, and the number of "positive" tests during the period of screening.

Several ratios relating input to output (or cost-effectiveness) are thus presented from the combination of parameters described.

It would be possible to carry out a more formal cost-effectiveness study using the output data from the simulation model. The framework for doing so has been presented by Blumberg (1957) and recently restated by Simpson et al (1978). This involves calculating the net value of screening, given the numbers of individuals who screen true positive, false positive, true negative and false negative, and the values imputed to these four states. True positive and true negative tests have positive values, false positives and false negatives have negative values (the consequence of unnecessary follow-up and misplaced reassurance respectively). This more detailed approach has not been used, in part because of the need to reach arbitrary decisions on the values of screening outcomes (the different cost-effectiveness ratios resulting from

different assumptions is a modelling exercise in its own right), and in part because the model generates ultimate outcomes (cases, deaths, life-years lost) rather than just screening test results.

3.1 COMPARISON OF NATURAL HISTORIES

As described in section VI, three natural histories were examined. The characteristics of these are set out in Appendix 3, Tables IV.16-18 and Figs 4.4 and 4.5. In 11M, cis is a rather stable condition, regressions are reduced to a low level. The median sojourn time of cis is 9.9 years, the distribution being exponential in format. In 11N cis is more transient, with a greater flux in and out of dysplasia. The area under the sojourn time curve (Fig 4.5) is correspondingly larger, the median sojourn shorter, but the distribution remains exponential. In history 11O there is the same rate of flux between dysplasia and cis as in 11N, however the shape of the sojourn time distribution is quite different; there are no long-duration cis cases, although the median duration (9.5 years) is much the same as in 11M. Dysplasia is a less transient condition also.

The actual numbers of cancer cases, deaths and years of life lost which result from simulation of a 30 year period when no screening is carried out vary slightly between the three different natural histories. For this reason, the comparison of the effects of screening assuming these natural histories examines percentage change (rather than absolute numbers). Table V.4 shows the results of the same screening policy (examinations at ages 35,40,45,50,55,60, 65), test characteristics (70% sensitivity, 99,5% specificity) and follow-up loss (8% per year dysplasia, 4% per year cis, for 3 years) under the assumptions of two different attendance rates (80%, 45%; probability for all women equal) and the three different natural histories.

At both screening intensities it is noticeable that the differences in the results for the three natural histories are really rather small.

At 80% attendance the savings in cases, deaths and life years appear to be greatest for 11O and least with 11N. Since the number of tests performed is almost identical, the same effect is seen in the ratio of savings per 1000 tests. The number of positive tests is rather higher for history 11O. This might be anticipated from the shape of the curves of distribution of sojourn times (Figs 4.4 and 4.5) which indicate a relatively large number of dysplasias and carcinomas in-situ of short durations, so that prevalence of these conditions is likely to be less reduced by regular screening than the

more stable natural history of 11M. A higher prevalence would lead to more positive tests on screening. The savings of deaths and life-years per positive screening test is thus higher for 11M than 11O.

When attendance at the 5 yearly screening examinations falls to 45%, the results for natural history 11O (notably for deaths and life-years) appear much worse. This too is presumably related to the sojourn time distribution - since few cis cases have long sojourn times, at low rates of attendance, a greater proportion will be able to transit onward to clinical cancer without being detected.

Fig 5.9 plots the cumulative person-years of life lost for the 30 years of simulation, comparing the three natural histories (11M, 11N & 11O) both in the absence of screening and with the rather intensive policy (80% attendance rate) summarised above. This diagram illustrates that the reduction in life-years lost achieved by screening is not evenly spaced throughout the 30 years. In the first 10 years there is relatively little effect; thereafter the 'saving' increases progressively with time. This is the kind of result which would be expected, since screening interrupts the disease in the pre-clinical stages - it is only some years later that some of the individuals so detected (and successfully treated) would have died from clinical cancer if screening had not been instituted. Evaluation of actual screening programmes should make allowance for this lag time, and to expect an immediate effect in terms of mortality is unreasonable.

In the following examples illustrating the effects of different screening policies, a single natural history (11M) has been used for simplicity.

3.2 COMPARISON OF DIFFERENT PATTERNS OF ATTENDANCE

Table V.5 shows the results obtained by simulation in a population of 100,000 women over a 30 year period with the same screening policy as already described in 3.1 above, and with annual rates of attendance ranging from 15% to 90%. The probability of attending is equal for all individuals of the specified ages.

For each apparently equal step in attendance rates, there is a progressively smaller saving in cases, deaths and life-years saved. The diminishing return achieved by increasing attendance rate is seen more clearly in diagrammatic form in Fig 5.10 which plots the actual numbers of cases, deaths and person-years of life lost at the different attendance rates. The tendency of

the number of cases, deaths and life-years lost (and the savings in these parameters) to reach a plateau indicates that, with a schedule of five-yearly screenings, there will always be a proportion of clinical cancers which pass through their pre-invasive stages in less than five years. In the present example this relationship is complicated by a less than perfect detection of abnormalities on screening (70% sensitivity) and the escape of a small proportion of screen-detected cases from surveillance.

The number of screening tests carried out in the population is directly proportional to the attendance rate. The ratio of savings per 1000 tests therefore shows a reduction in yield with increasing attendance rates. However, this decline is less steep for the ratios shown under 'savings per positive test'. This is because the proportion of tests which are positive falls as the intensity of screening increases (from 20 per 1000 at 15% attendance to 16.3 per 1000 at 90% attendance). This is a consequence of a reduction in prevalence of preclinical lesions in the population as the intensity of screening increases.

In the results presented so far, the likelihood of attending for screening at the ages schedules (35,40,45,50,55,60,65) has been equal for all individuals in the population, at a probability defined by the attendance rate. Because of the stochastic nature of the model, the population simulated is examined as individuals, and transfer probabilities can be made dependent upon personal variables. In Table V.6 the effects of making attendance for screening dependent upon such variables are examined.

The simplest proposition is to suppose that 20% of women will never attend a screening programme when it is offered, The other 80% may attend, their attendance rate at each schedules test is 75%, so that the apparent rate of attendance in the entire population is 60%. As might be expected the results achieved (savings of cases, lives, life-years) are inferior to the situation, represented by 60% attendance for the entire population, but the programme costs (total tests, positive tests) are almost identical.

In section II.3.2 it has been described that attendance at screening programmes is not a random event, but is related to such variables as age, marital status and social class. It is quite clear, for instance, that women who do not attend for screening are at higher risk of cervix cancer than those who do attend. The second column of Table V.6 represents the situation where attendance for screening tests is only half as likely in women with abnormalities of the cervix (dysplasia, cis, micro-invasive/occult invasive

disease). The overall attendance is 80%, and a comparison with the position where probability of attendance is the same for all individuals shows that the 'saving' are reduced by about one quarter. There are naturally considerably fewer positive tests, of which a greater proportion are now false-positives. The overall outcome is a reduction in savings per 1000 tests, but savings per positive test are likely affected.

In the same table, the effect of making probability of attendance depend upon marital state is shown. The ratios chosen are 5 : 9 : 2 for single : married : formerly married. This was the approximate ratio seen in the Leeds - Wakefield study (Parkin et al, 1981) - see Table II.12. Once again overall attendance in the whole population is close to 80%. Because women in the formerly-married group have elevated rates of onset of dysplasia (See Appendix 3), so that prevalence of precursor conditions will be highest in this group, their poorer attendance results in small reductions in savings and in positive tests. The ratios savings per 1000 tests and savings per positive test are slightly below those seen when a random 80% of women attend for screening.

Table II.12 also shows that attendance for screening examinations tends to decrease with age. Table V.6 (last column) shows a simulation of 30 years screening where the rate of attendance falls from 60% at age 35 to 30% at age 65. This is compared with a similar overall rate of examination - 45% at all ages. The savings of cases, deaths and life-years are less when screening attendance falls off with age, even though there is a slightly increased proportion of positive screening examinations. The explanation is probably the higher prevalence of precursor lesions in younger women (Figs 5.5. and 5.6) so that yield of positives is higher when attendance is greater at young ages, but that this is offset by the more rapid progression of carcinoma in-situ in older women (see Table IV.6), so that failure to interrupt the course of such lesions by screening has greater consequences in terms of clinical cancer.

3.3 TEST CHARACTERISTICS AND FOLLOW-UP

Table V.7 examines the effects of varying two parameters, success of follow-up and test characteristics, on the results of the screening programme summarised (examinations at exact ages 35,40,45,50,55,60,65; 80% of the population attend on each occasion).

3.3.1 Follow-up intensity

It is known that in any screening programme a proportion of individuals with precursor lesions who are found to have positive cytology will not be

removed from the risk of developing clinical cancer. This may be because follow-up is inadequate (the individuals do not attend for further screening tests, or for diagnostic biopsy) or because such follow-up procedures (e.g. regular 6 monthly cytology, or treatment by laser or cone biopsy) may themselves be inadequate. In the policies examined in the results section the usual assumption is that screen-detected dysplasias escape surveillance (revert to dysplasia) at a rate of 8% per year for 3 years (equivalent to one fifth of the cases detected). For cis the loss is only half of this (since it is assumed that the cytological features at screening would prompt more intensive follow-up of the case). Table V.7 examines two other possibilities which envisage more successful surveillance - a loss of only 2% of detected dysplasia and 1% detected cis cases for a 3 year period (5% and 2.5% lost overall), and a perfect system where, once detected by screening, the individuals concerned have no further possibility of developing cancer.

The results show that, as the quality of follow-up deteriorates so too do the savings achieved (cases, lives, life-years), and there is a small increase in the number of tests carried out (fewer people are successfully treated or under permanent surveillance) and in the proportion of screening tests that are positive (since the prevalence of precursor lesions which are not treated or under follow-up will increase). Nevertheless, within the range examined here the differences in savings achieved and in the ratio of savings to tests are rather small.

3.3.2 Screening test characteristics

As discussed in section II.3.2 screening test performance can be described in terms of sensitivity and specificity, and these bear a reciprocal relationship to each other. In the programmes presented in this results section a test sensitivity of 70% and specificity of 99.5% (5 per 1000 false positive rate) has been assumed. These values are approximately equivalent to those which have been estimated from the results of screening programmes (section II.3.2.1). In Table V.7 two other possibilities are examined. One envisages a higher sensitivity (90%) achieved presumably by the classification as 'abnornal' of minor degrees of cytological change, which would lead to a decrease in specificity (to 99%). The other alternative examines the opposite effect of increasing specificity (to 99.9%) at the cost of a loss of sensitivity (to 50%).

The results indicate that the savings in cases, lives and life-years increase in direct proportion to the test sensitivity. Since the total number of tests carried out will remain the same, the savings per 1000 total tests

shows the same effect. The number of positive tests on screening shows an even steeper increase, however, because the increasing sensitivity is accompanied by a decreasing specificity, and this leads to large numbers of false positives. The result is that the ratio of savings per positive test for the three different sets of test characteristics, are in the opposite direction from the savings per total tests.

Supposing that it were possible to choose the precise characteristics of the screening test, the optimum could be selected by comparing the costs and benefits of the different options. Cost could be derived from the relative expense of negative screening tests (cost of taking and examining a smear) and of true and false positive tests (which demand follow-up and possible treatment). Benefit would be derived not only from the person-years of life saved, but also from the number of cases of cancer avoided, since there is an obvious benefit from avoiding treatment for clinical cancer, even though the outcome is successful in terms of survival.

3.4 COMPARISON OF DIFFERENT SCREENING POLICIES

Table V.8 examines the outcome of several screening policies over a 30 year period.

The screening policy of five yearly examinations between the ages of 35 and 65 has been presented in two different ways. In column 1 is the policy used many times already, of offering tests at exact ages 35,40,45,50,55,60,65. The fourth column represents the effect of introducing a policy which calls for all women to present for tests at five yearly intervals. The overall number of examinations and positive tests with these two schedules is almost identical, but their distribution over time is very different. Fig 5.11 illustrates this. For the 5 yearly schedule, in year one all 30,000 women aged 35-65 are tested, in the next four years only those attaining age 35 are eligible. At year 6 all women aged 40-65, and those exactly 35 become eligible for screening, and for the next four years so do women reaching ages 35 and 40. The oscillations gradually decrease so that the number of tests annually tends to become constant. With the schedule testing women at exact ages, the annual number of tests remains almost constant. The results of the 5-yearly interval policy appear to be slightly better than that of tests at exact ages. This may be because of more intensive examination at older ages in the first year of the simulation.

Columns 2 and 3 of Table V.8 illustrate possible modifications to the exact ages policy to increase efficiency. Not examining women who are either single or who have had no children reduces the number of tests required in the 30 years of simulation by 20% (to 153,000), and increases the proportion of screening tests which are positive (from 16.7 per 1000 to 18.2 per 1000). However, the decrease in savings of cancer cases, deaths and life-years lost means that the outcomes to cost ratios are either the same as (savings per 1000 tests) or inferior to (savings per positive test) those obtained by screening the whole population.

Since dysplasia is assumed to be a rather transient lesion, the great majority of which regress to normality, the effect of ignoring screening tests showing minor degrees of abnormality (consistent with dysplasia) has been examined. There is a large reduction in positive tests (most of which are false positives). However, failure to follow-up dysplasias leads to a reduction in the savings achieved, so that although the ratios of savings per positive test are improved, the ratios of savings per 1000 tests are worse. Whether such a policy is worthwhile depends on the relative costs imputed to negative tests and to true and false positives and a comparison with the benefits obtained.

The final column examines the results obtained by examining women only at the time of pregnancy. The rationale for such a policy would be the lower cost of the tests (especially negative tests) since, as the tests can be taken incidental to other health-service attendances, no special screening service needs to be established. It can be seen that the savings with such a schedule are much less than those achieved by the other policies. However, because of the young age at which testing is performed, the saving of life-years is less inferior than the other two parameters. The savings per 1000 tests and savings per positive test are inferior to those achieved by regular examination at older ages. However, if the cost of a negative test taken during ante-natal or post-natal care was only half that taken at special screening clinics, then a favourable cost-benefit ratio is seen for pregnancy screening if benefit is equated with life-years saved, and the cost of follow-up and treatment of positive tests is up to one-hundred times that of a negative test. Thus, even though the yield is rather small, pregnancy screening may be a relatively efficient way of deploying resources.

Table V.9 summarises five screening policies which have been recommended for England and Wales, and which have been described in more detail in section II.3.2.2.

Table V.10 illustrates the simulated outcome of applying these policies (1 to 5) to a population with the structure of that of England and Wales for the thirty year period 1961-1990. For all these policies, very favourable rates of attendance have been assumed; a random 80% of females attending all the routine tests.

In the British Society of Clinical Cytology recommendations (3 and 4) the onset of routine testing is after the age of 25 at the time of attendance for pregnancy, contraceptive advice, or venereal disease. In the simulation a start to screening at the time of pregnancy (childbirth) is readily modelled, but there is no data available on the probability of attendance for contraception/v.d. between ages 25 and 29. The arbitrary solution adopted was to make the annual probability 0.2 for individuals with a normal cervix and 0.4 for individuals with precursor lesions (in keeping with the increased prevalence of abnormality in contraceptive users and patients with venereal disease). A similar problem exists in modelling the Committee on Gynaecological Cytology recommendations (policy 5). The solution adopted was to postulate (generously) a 50% probability of receiving a first test at ages 22 and 23, and a 50% probability of being screened at age 30 if no test had been taken in the preceding five years. Attendance in women with abnormal cervices (dysplasia, cis, micro/occult invasive) was increased to 67% in keeping with an increased risk of disease in contraceptive users (this rate results in prevalence being double that in normal subjects).

The results indicate that the highest yield in terms of savings is achieved with the policy involving 3 yearly routine tests (policy 4), but that this involves the greatest number of screening tests. The yield, particularly in terms of lives and life-years saved, is rather similar for policies 2,3 and 5. However, the input of screening tests is considerably different, so that the savings per test ratios are much less favourable for the more intensive policies. It should be pointed out that the costs per screening test are probably not identical for all these policies, in particular with the C.G.C. policy (number 5). Some 89,000 tests were taken during pregnancy and a further 26,000 during attendance for family planning, and such examinations taken incidental to other procedures may be less costly than examination at special screening sessions. Similarly, with the BSCC policies, a small proportion of tests are carried out incidental to pregnancy, contraception or venereal disease attendance (About 9500 per year). Table V.II shows a rather crude cost-effectiveness analysis of these five policies, using as a measure of output the life-years saved over the first 30 years of screening. The unit of cost is taken to be that of a routine screening test; examinations taken

incidental to another procedure are taken to cost half this amount. The cost of follow-up of a false positive (usually involving repeat smears) is taken to be five times, and the cost of diagnosing and treating true positives twenty times that of a routine smear. The efficiency of the Committee for Gynaecological Cytology policy (number 5) is considerably enhanced using this approach when compared with the simple savings per test analysis of Table V.10. Nevertheless the yield of screening appears to little superior to the policy it was designed to replace (number 2) and the cost-effectiveness is clearly inferior.

VI CONCLUSIONS

The model which has been developed meets many of the specifications which were laid down during the discussion on the problems involved in evaluating different screening policies. It is simple in conception and easy to understand, since the approach adopted was to produce a model which was lifelike, albeit clumsy, rather than abstract and sophisticated. The demographic basis of the model, following a total population for a relatively short time period, is a much more satisfactory background for studying screening that the single-cohort method. The disease process is simulated by what is essentially a simple markov-process, but the lack of time-dependence is avoided by the device of multiplying the number of disease states by a set of durations to produce states of disease/duration, from which transfer rates are specified. This allows a great deal of flexibility in defining natural histories. Disease natural history can be modified by individual characteristics (in the examples given, marital status and parity were used), as can behaviour with regard to screening. Finally, the pattern of screening activity which can be superimposed on the population is extremely flexible, and is not limited to the highly theoretical policies which have been examined in the past.

The input data from the model are based on real observation, wherever this is feasible, so that it should be possible to verify the model output against the actual population results. This has been done for the demographic component, and to some extent for the natural history. However, to date there has not been an attempt to verify whether the trends in disease observed in England and Wales could be reproduced by simulating the screening activity that has taken place. It is lack of accurate knowledge about this activity that is a major limiting factor, nevertheless this is an area which merits some future effort.

The other general area where validation studies are possible is that of natural history. This is very important, since it is the more or less arbitrary choice of natural history parameters that makes much simulation work unconvincing (see, for example, Chamberlain, 1982). The specification of natural histories in the present study was based on data on cross-sectional prevalence and incidence rates, and on observational studies of pre-invasive disease. The results of simulation did not appear to be very sensitive to the choice of natural history. The joint IARC/WHO collaborative programme on the evaluation of screening programmes for cancer of the uterine cervix has brought together available material from different screening programmes

(mainly in Scandinavia) on the rates of disease onset at varying time-periods after one or more negative screening tests. Interpretation of this material in terms of natural history is not easy, but it offers the opportunity of testing whether the same order of results can be achieved using simulations based on the natural histories derived as described above.

The potential for simulating complex screening programmes with this type of model has been demonstrated. It is the author's belief that it is not possible or necessary to separate screening tests into incidental (sometimes called "diagnostic") and routine ("mass" screening). Testing at the time of other contacts with the health care system (eg pregnancy, gynaecology attendance) is a fairly satisfactory and efficient way of reaching relatively high risk groups who may otherwise not attend for screening. A screening programme should seek to add a set of special screening examinations to this background service. There is a need for good data on attendance rates and population coverage of gynaecology clinics and family planning services which can be used by the simulation model to examine these possible options.

There is ample scope for improving the technical aspects of the type of model described. A more efficient computer solution is almost certainly possible which will retain the essential features of the model (a micro-simulation which involves examination of the members of a mixed population over a short time period). The stochastic nature of the model means that outputs from simulations using identical parameters will not be the same, and to produce stable results when rare events are under study large populations have to be simulated. This uses large amounts of computer time (1 1/2 - 2 hours of C.P.U. time are needed on the VAX computer at IARC to study a population of 100,000 for 30 years). Improvement on this is almost certainly possible; but even without it the model provides a more feasible means of studying the effects of different screening programmes than the use of clinical trials!

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TABLE II.1

Age-adjusted Death Rates of Cancer by Site and Year (1970-1975)
Cervix uteri (female)

Country	1970	1971	1972	1973	1974	1975
Africa						
1. Egypt	0.33	0.28				
2. Mauritius	7.66	7.60	7.47	4.48	5.92	
3. South Africa						
America						
4. Canada	5.70	5.39	4.95	4.46	4.37	3.68
5. Chile	15.53		15.34	16.68	16.10	15.37
6. Costa Rica	10.02	11.20	7.69	12.42	10.89	9.01
7. Cuba		5.41	4.86	4.72	4.63	5.66
8. Dominican Republic				3.90	3.28	4.81
9. Ecuador		4.04		5.14	7.27	
10. El Salvador	6.55	4.97	4.94	3.61	4.43	
11. Honduras	0.71		0.42			0.26
12. Martinique					4.97	4.79
13. Mexico	10.30		10.57	11.25	11.20	
14. Nicaragua				1.03		
15. Panama	11.16	7.72	15.52	10.00	8.10	
16. Paraguay				10.49		12.95
17. Puerto Rico		5.79	4.83	4.14	4.89	4.44
18. Trinidad & Tobago		16.43		15.32	17.97	11.39
19. United States	5.60	5.12		4.56	4.42	4.02
20. Uruguay		5.79	7.40	6.06	4.91	5.43
21. Venezuela	12.65	13.48	11.78	12.09	12.64	11.19
Asia						
22. Hong Kong	7.88	8.51	8.47	8.15	7.78	7.23
23. Israel	1.10	0.83	1.54	1.86	1.78	2.16
24. Japan	2.54	2.41	2.50	2.20	2.32	2.34
25. Philippines				1.20	1.25	1.19
26. Singapore	9.10	9.95		9.30	9.69	6.00
27. Thailand	0.70	0.56	0.53	0.84	0.80	0.71
Europe						
28. Austria	4.68	4.95	5.21	5.34	5.21	4.78
29. Belgium	3.59	3.96		3.33	2.97	2.61
30. Bulgaria	2.98	2.55	2.98	3.21	3.00	2.84
31. Czechoslovakia	5.46	5.49	5.33	5.46	5.01	5.18
32. Denmark	8.99	10.53	8.42	8.47	8.62	8.11
33. Finland	4.53	5.03	3.79	3.16	3.28	2.98
34. France	2.44	2.55	2.48	2.52	2.57	2.40
35. Germany, F.R.	5.80	5.80	5.75	5.84	5.70	5.50
36. Greece	0.82	0.88	1.09	1.30	0.66	0.84
37. Hungary	6.46	6.10	6.72	6.48	6.50	6.50
38. Iceland		7.99	5.14	2.38	7.65	6.23
39. Ireland	4.16	3.42	4.18	4.25	2.64	3.91
40. Italy	1.58	1.50	1.33	1.31	1.15	
41. Luxembourg	3.93	7.85	4.74	7.28	3.64	
42. Malta	4.27	3.17	1.83			
43. Netherlands	5.33	5.32	4.89	4.33	4.86	4.54
44. Norway	6.34	6.11	5.27	5.80	4.72	5.75
45. Poland	8.56	9.33	9.30	9.26	8.74	8.63
46. Portugal	8.68	8.05	7.01	6.49	6.76	4.98
47. Romania	9.31	9.63	9.55	9.87	10.20	
48. Spain	0.82	0.69	0.83	0.67	0.82	0.82
49. Sweden	5.98	5.03	5.10	4.95	4.43	4.33
50. Switzerland	5.90	6.25	5.28	5.41	4.93	5.02
51. England & Wales	6.08	6.06	5.73	5.87	5.27	5.53
52. Northern Ireland	5.06	4.00	5.06	5.13	3.63	5.02
53. Scotland	6.03	5.84	5.31	6.13	5.06	6.04
54. Yugoslavia	6.37	4.98	4.87	4.89	4.88	4.26
Oceania						
55. Australia	5.16	4.80		5.01	4.83	4.50
56. New Zealand	5.67	5.84	5.18	5.24	5.56	5.23

Source : Segi et al (1981)

TABLE II.2

CHANGES IN MORTALITY FROM MALIGNANT NEOPLASM OF UTERUS AT AGES 35-64, 1955-59, 1965-69

VARIATIONS DE LA MORTALITÉ PAR TUMEUR MALIGNE DE L'UTÉRUS POUR LE GROUPE D'ÂGE 35-64 ANS, 1955-59, 1965-69

	Standardized rates per 100 000 — Taux normalisés pour 100 000						Existence of marked downward trend in mortality from M.N. Cervix Existence d'une régression marquée de la mortalité par tumeur maligne du col de l'utérus		
	Specified Cervix — Col de l'utérus			Total Uterus — Utérus général					
	1955-59	1965-69	% change variation en %	1955-59	1965-69	% change variation en %	Probable	Possible	Improbable
AMERICA — AMÉRIQUE									
Canada	17.5	13.3	— 24	26.1	19.1	— 27	•		
Chile — Chili	19.0	29.3	+ 54	43.7	43.7	0			•
United States — Etats-Unis	19.0	13.5	— 29	29.1	19.8	— 32	•		
Venezuela	25.2	29.2	+ 16	69.9	56.8	— 19			•
ASIA — ASIE									
Israel — Israël	2.0	2.4	+ 20	12.3	9.5	— 23		•	
Japan — Japon	7.0	7.2	+ 3	39.8	25.9	— 35		•	
EUROPE									
Austria — Autriche	7.4	10.5	+ 42	44.0	36.3	— 18		•	
Belgium — Belgique	14.6	7.8	— 47	33.8	22.8	— 33		•	
Czechoslovakia — Tchécoslovaquie	14.8	14.0	— 5	32.1	24.8	— 23		•	
Denmark — Danemark	24.8	27.5	+ 11	39.9	35.5	— 11			•
Finland — Finlande	12.0	11.9	— 1	24.8	18.9	— 24		•	
France	6.6	6.6	0	26.0	22.1	— 15		•	
Germany, Fed. Rep. of Allemagne, Rép. féd. d'	8.8	13.5	+ 53	28.7	27.1	— 6			•
Hungary — Hongrie	6.4	12.6	+ 97	47.3	35.5	— 25		•	
Ireland — Irlande	5.9	8.6	+ 46	19.6	16.8	— 14			•
Italy — Italie	4.3	4.0	— 7	30.1	26.9	— 11			•
Netherlands — Pays-Bas	13.9	13.1	— 6	21.9	20.3	— 7			•
Norway — Norvège	16.7	13.4	— 20	22.6	18.5	— 18	•		
Portugal	20.8	17.7	— 15	30.0	25.4	— 15	•		
Sweden — Suède	10.6	13.9	+ 31	22.2	19.8	— 11			•
Switzerland — Suisse	15.9	11.7	— 26	25.5	20.7	— 19	•		
U.K.: England and Wales R.-U.: Angleterre et Galles	15.2	15.1	— 1	21.7	20.7	— 5			•
U.K.: Northern Ireland R.-U.: Irlande du Nord	11.7	12.3	+ 5	21.9	18.4	— 16		•	
U.K.: Scotland — R.-U.: Ecosse	15.2	15.5	+ 2	25.6	21.2	— 17		•	
OCEANIA — OCÉANIE									
Australia — Australie	12.1	11.6	— 4	19.4	15.8	— 19	•		
New Zealand — Nlle-Zélande	15.9	13.1	— 18	22.5	18.2	— 19	•		

Source : Hill (1975)

TABLE II.3

MORTALITY RATES, PER MILLION, ENGLAND & WALES,

1955-1980

	AGE GROUP					
YEAR	25-34	35-44	45-54	55-64	65+	ALL AGES
1955	24	84	156	255	313	108
1956	27	81	165	235	322	108
1957	24	96	153	224	312	106
1958	23	103	178	246	326	115
1959	23	103	163	210	318	108
1960	20	109	183	227	314	109
1961	19	92	160	215	289	104
1962	10	106	174	200	293	104
1963	11	99	178	193	282	101
1964	10	105	202	188	291	105
1965	11	104	192	200	255	100
1966	9	91	176	196	290	100
1967	10	84	189	198	258	99
1968	11	76	202	201	242	98
1969	11	70	182	197	258	97
1970	11	59	184	203	239	94
1971	14	65	189	195	227	92
1972	15	58	166	201	218	88
1973	12	49	174	207	222	89
1974	15	44	141	184	220	82
1975	20	49	135	207	216	85
1976	18	47	143	230	212	88
1977	21	60	136	195	216	85
1978	27	58	125	197	219	85
1979	24	59	111	200	211	83
1980	30	56	110	190	209	82

Sources : 1) Cancer Mortality : England and Wales 1911-70. Studies on Medical and Population Subjects no 29 HMSO, 1975

2) Roberts (1982)

TABLE II.4

INCIDENCE (REGISTRATION RATES) PER 100,000, ENGLAND AND WALES

(Excludes in-situ lesions)

	AGE GROUP							
YEAR	15-24	25-34	35-44	45-54	55-64	65-74	75+	ALL AGES
1962	0.2	4.6	29.1	35.2	30.9	32.4	25.4	17.2
1963	0.3	5.4	29.1	35.9	32.9	31.0	28.5	17.9
1964	0.3	4.9	29.5	39.6	33.5	30.6	30.6	18.4
1965	0.4	5.3	30.6	40.7	34.7	30.7	28.1	18.4
1966	0.4	5.7	29.2	41.0	33.4	31.9	25.1	18.1
1967	0.4	5.1	25.8	43.7	33.6	31.1	29.3	18.0
1968	0.4	5.8	24.4	42.1	33.0	28.9	25.3	17.2
1969	0.7	6.5	20.5	37.9	32.6	29.9	24.8	16.3
1970	0.4	7.0	20.1	38.7	35.3	28.0	22.4	16.3
1971	1.0	8.6	19.6	39.7	31.4	26.8	25.8	16.3
1972	1.0	7.6	16.7	35.1	35.0	27.4	24.1	15.6
1973	0.7	9.2	17.4	33.8	37.0	28.2	25.4	16.1
1974	0.9	9.8	15.7	32.1	37.5	29.3	26.1	16.0
1975	0.8	9.5	17.3	30.9	37.1	29.4	26.0	16.0
1976	0.9	10.6	16.6	29.4	37.6	27.8	25.0	15.7
1977	1.3	12.0	17.2	27.6	36.9	30.0	24.0	15.9
1978	1.3	12.8	18.4	24.1	34.5	28.2	23.7	15.4
1979	1.0	13.5	19.4	22.9	34.0	29.7	22.6	15.4
1980	1.3	14.6	21.7	22.5	36.3	29.5	24.8	16.2

Sources : 1) Registrar Generals Statistical Review of England and Wales : Supplements on Cancer (years 1962-1970)

2) OPCS : Cancer Statistics, Registrations MB1 nos 1,2,4,5,7,8,9 (years 1971-1978)

3) OPCS : Cancer Registrations 1979, and 1980 (estimates) MB1 83/1

TABLE II.5

REGISTRATIONS OF CARCINOMA IN SITU OF THE CERVIX

IN ENGLAND & WALES

RATES PER MILLION WOMEN

YEAR	Age-group					
	15-24	25-34	35-44	45-54	55-64	65+
1965	8	103	198	109	32	14
1966	19	168	300	167	37	13
1967	23	230	406	242	52	15
1968	33	249	365	225	44	14
1969	36	268	313	201	51	15
1970	35	237	252	164	41	12
1971	38	256	244	148	40	9
1972	54	251	235	157	46	16
1973	53	309	277	132	54	12
1974	65	387	296	152	48	13
1975	73	419	316	149	47	16
1976	85	504	346	143	53	20
1977	88	549	402	151	53	15
1978	89	552	398	140	47	12
1979	82	627	417	145	51	17
1980	109	710	468	174	70	19

TABLE II.6

ESTIMATED NUMBERS OF SMEARS AND REGISTRATIONS OF CARCINOMA IN SITU IN ENGLAND AND WALES

NUMBER OF CASES AND RATES PER 1000 SMEARS

AGE												
LESS THAN 25 YEARS				25-29			30-34			35 and over		
YEAR	Smears '000s	CIS Regns	Rate per 1,000 smears	Smears '000s	CIS Regns	Rate per 1,000 smears	Smears '000s	CIS Regns	Rate per 1,000 smears	Smears '000s	CIS Regns	Rate per 1,000 smears
1973	487	179	0.37	455	480	1.05	328	522	1.59	1068	1399	1.31
1974	560	220	0.39	490	648	1.32	354	626	1.77	1072	1497	1.39
1975	592	248	0.42	482	713	1.48	380	688	1.81	1044	1536	1.47
1976	566	293	0.52	476	820	1.72	429	900	2.10	1097	1621	1.48
1977	616	309	0.50	458	890	1.94	385	1004	2.61	1086	1766	1.63
1978	600	316	0.53	441	904	2.05	383	1012	2.64	1163	1702	1.43

TABLE II.7

Number Studied and Per Cent of Subjects with Positive Antibody Titers to Herpes Genitalis In Recent Case/Control Studies of Cervical Cancer and Its Precursors

Area and Study	Invasive Carcinoma					Carcinoma In Situ					Dysplasia				
	Cases		Controls			Cases		Controls			Cases		Controls		
	NUMBER	PER CENT	NUMBER	PER CENT	RR*	NUMBER	PER CENT	NUMBER	PER CENT	RR	NUMBER	PER CENT	NUMBER	PER CENT	RR
India (Seth et al, 1978)	146	64.5	116	36.2	3.2										
Maryland (Thomas and Rawls, 1978)		/				75	57.3	132	37.1	2.3	84	44	132	37.1	1.3
Maryland (Royston and Aurelian, 1970)	42	100	42	67	∞	32	100	32	52	∞	36	95	36	44	24.2
Belgium (Sprecher-Goldberger, 1971)	30	83	46	33	9.9										
Chicago (Plummer, 1971)	27	30	44	9	4.3										
Houston (Adam et al, 1972)	60	52	290	28	2.8	62	39	290	28	1.6	137	31	290	28	1.2
Barbados (Ory et al, 1974)	35	97	59	77	10.4										
Boston (Catalano and Johnson, 1971)						45	42	90	18	3.3					
Finland (Peltonen, 1975)															
Houston (Rawls et al, 1973)	85	70	51	22	8.3	29	38	51	22	2.2	23	28	51	22	1.3

*Relative risk calculated by exposure odds ratio $\frac{Pca\,(1 - Pco)}{Pco\,(1 - Pca)}$ where Pca is per cent of cases with positive antibodies and Pco is per cent of controls.

Source : Cramer (1982)

TABLE II.8

RESULTS OF BRITISH COLUMBIA COHORT STUDY

Boyes et al. (1982)

ESTIMATED PREVALENCE AT FIRST CONTACT

Age-group	Prevalence, per 1000: Carcinoma in situ (or worse)	Prevalence (per 1000) allowing for false negative tests: dysplasia (or worse)	Prevalence (per 1000) allowing for false negative tests: c.i.s. (or worse)
20-24	(5.1)	(6.7)	(5.6)
25-29	6.8	8.0	7.6
30-34	10.6	14.2	11.9
35-39	10.7	14.0	12.6
40-44	11.0	12.8	12.3
45-49	9.6	12.0	10.7
50-53	7.3	9.8	8.1

ESTIMATED INCIDENCE RATES (PER 1000)

Age-group	Dysplasia (or worse): Method I*	Dysplasia (or worse): Method II+	C.I.S. (or worse): Method I*	C.I.S. (or worse): Method II+
25-29	1.46	0.31 - 1.34	0.98	0.31 - 1.03
30-34	1.37	1.27 - 1.60	1.04	0.98 - 1.21
35-39	0.78	1.19 - 0.63	0.36	0.69 - 0.29
40-44	0.60	0.30 - 0.80	0.46	0.13 - 0.53
45-49	0.91	0.61 - 0.78	0.60	0.43 - 0.51
50-54	0.63	0.93 - 0.46	0.32	0.39 - 0.20

* Method I : Calculation excludes the data most affected by carry over of false negatives from initial examination(s)

+ Method II : Data allows for false negative rate on initial and subsequent examinations (10.8% for dysplasia, 9.6% for c.i.s.) ; figures represent dating of incidence as first abnormal smear, or as midpoint between smears.

TABLE II.9 Screening workload in England and Wales

Table 1: *Estimated total smears (thousands) and (in parentheses) positive cases per 1 000 smears examined by source*

Year	General Practitioners	Area[1] (Local) Health Authority	Family Planning Clinics	Hospital Clinics	Other Clinics	All sources
1965[2]	64	81	78	428	36	687
1966[2]	183	354	149	509	68	1263
1967[2]	245	384	141	521	51	1342
1968	313	378	168	551	58	1467 (6·3)
1969	363	388	227	587	67	1632 (5·7)
1970	419	431	284	620	82	1835 (4·7)
1971	477	433	345	649	90	1995 (4·4)
1972	539	473	376	640	96	2124 (4·5)
1973	630 (3·5)	541 (2·4)	411 (2·1)	552 (9·8)	204 (1·7)	2338 (4·3)
1974	785 (3·7)	624 (2·5)	518 (2·6)	477 (11·3)	72 (4·9)	2476 (4·7)
1975	814 (3·8)	628 (2·4)	455 (3·2)	423 (13·1)	179 (2·0)	2498 (4·8)
1976	942 (3·9)	627 (2·5)	423 (3·5)	445 (13·8)	129 (3·4)	2568 (5·2)
1977	952 (4·6)	605 (2·4)	389 (4·3)	501 (14·2)	98 (4·0)	2545 (5·9)
1978	958 (4·8)	628 (2·8)	388 (4·5)	528 (14·7)	85 (4·4)	2587 (6·3)
1979	1065 (4·7)	704 (2·6)	374 (5·1)	549 (14·8)	57 (7·4)	2749 (6·3)
1980	1252 (5·0)	708 (2·7)	356 (5·9)	570 (16·0)	42 (13·1)	2928 (6·8)

Table 2: *Estimated total smears (thousands) and (in parentheses) positive cases per 1 000 smears examined by age groups*

Year	Age group (years)				
	Under 25	25-29	30-34	35 and over	All ages
1973	487 (1·8)	455 (3·5)	328 (4·5)	1068 (5·7)	2338 (4·3)
1974	560 (2·5)	490 (4·2)	354 (5·6)	1072 (5·9)	2476 (4·7)
1975	592 (2·1)	482 (4·5)	380 (5·5)	1044 (6·2)	2498 (4·8)
1976	566 (2·4)	476 (5·1)	429 (6·1)	1097 (6·3)	2568 (5·2)
1977	616 (2·5)	458 (6·0)	385 (7·8)	1086 (7·1)	2545 (5·9)
1978	600 (2·8)	441 (7·3)	383 (9·3)	1163 (6·7)	2587 (6·3)
1979	632 (2·6)	467 (7·2)	406 (9·7)	1244 (6·7)	2749 (6·3)
1980	701 (3·0)	469 (8·6)	404 (11·4)	1354 (6·8)	2928 (6·8)

[1] Local Health Authority prior to 1974 NHS re-organization.
[2] 1965, 1966 and part 1967 figures are based on a sample.

NOTES TO TABLES 1 and 2:–

(1) Prior to 1973 information on source of smear was obtained from pathology laboratories; detection rates are not available. Since then the number of smears examined by source and age have been estimated from a 20% sample of negative smears taken during January and July of each year and returned to the National Health Service Central Register.
(2) The total number of positive cases is obtained from the laboratory return SBH 140.
(3) Because of rounding the sum of figures across a row may not equal the "All sources" figure.

Source : Roberts (1982)

TABLE II.10

Estimated total smears by age and source, 1980

Age (years)	Smears	General Practitioners	Area Health Authority Clinics	Family Planning Clinics	Hospital Clinics	Other Clinics	All sources
Under 25	Estimated total smears	270000	133000	150000	140000	8000	701000
	Detection rate	2·0	1·2	2·2	7·1	12·8	3·0
25-29	Estimated total smears	189000	80000	73000	119000	7000	469000
	Detection rate	5·9	4·3	8·2	15·5	17·2	8·6
30-34	Estimated total smears	170000	79000	52000	98000	5000	404000
	Detection rate	8·6	6·0	11·9	19·8	20·2	11·4
35 and over	Estimated total smears	622000	417000	80000	212000	23000	1354000
	Detection rate	5·0	2·3	6·6	20·7	10·2	6·8
All ages	Estimated total smears	1252000	708000	356000	570000	42000	2928000
	Detection rate	5·0	2·7	5·9	16·0	13·1	6·8

NOTE: (1) The number of smears examined by source and age group is estimated from a 20% sample of negative smears taken during January 1980 and July 1980 and returned to the National Health Service Central Register. The number of positive smears and the total number of smears are from form SBH140.

(2) Detection rate = Positive cases per 1 000 total smears.

(3) Because of rounding the figures down a column or across a row may not equal the "All ages" or "All sources" figure.

TABLE II.11

Cytology testing 1976–1977: place of examination

Place of testing	Tests performed		Persons examined						
					Age		Contraception		
	No.	(%)	No.	(%)	Mean	% under 35	Taking pill	I.U.C.D.	% With symptoms*
General practitioner	24,800	(25·5)	22,800	(27·8)	35·7	51·2	32·1	3·0	30·9
Health authority clinics	18,910	(19·3)	18,040	(22·0)	41·2	28·9	20·4	1·5	17·0
Family planning clinics	19,040	(19·6)	16,040	(19·6)	28·1	80·9	52·8	13·5	15·9
Ante-natal clinics	10,870	(11·2)	9,550	(11·7)	25·7	92·8	0·2	0·2	—
Post-natal clinics	2,240	(2·3)	1,730	(2·1)	27·8	87·7	15·9	2·4	—
Gynaecology out-patients	16,030	(16·5	9,630	(11·8)	37·7	45·0	18·5	4·3	79·7
Hospital in-patients	790	(0·8)	440	(0·5)	37·2	51·9	13·0	(0)†	80·4
Outreach clinics									
W.N.C.C.C.	420	(1·0)	800	(1·0)	39·3	40·1	20·9	(0)	14·3
A.H.A. factory visits	530								
Special (V.D.) clinics	2,540	(2·6)	1,810	(2·2)	25·1	88·0	54·3	(0)	54·6
Private patients	1,080	(1·1)	1,050	(1·3)	41·8	37·5	(0)	3·9	100
Total	97,250	(99·9)	81,890	(100)	34·2	57·4	27·4	4·4	33·8

* Excludes pregnant and post-natal women. † (0) too few for reliable estimate.

TABLE II.12

Attendance for cytology testing in relation to age

Age	Attendances		% first attendances	Annual attendance rates (100)			Total
	No.	(%)		Single	Married	Widowed/divorced	
15–19	6,350	(6·5)	65·8	6·2	24	(—)	7·5
20–24	17,610	(18·1)	40·7	19·4	24·4	31·6	22·3
25–29	18,000	(18·5)	23·6	17·0	22·7	16·3	21·6
30–34	15,370	(15·8)	16·6	9·2	21·5	10·4	20·0
35–39	11,440	(11·8)	14·0	8·8	18·7	11·8	17·7
40–49	16,250	(16·7)	15·0	4·5	13·5	10·6	12·8
50–59	8,540	(8·8)	17·1	2·9	7·0	3·4	6·3
60+	3,690	(3·8)	28·9	0·04	2·4	0·8	1·4
All ages	97,250	(100·0)	23·9	8·2	13·5	2·9	10·6

Trends in Incidence of Invasive Cervical Cancer per 100,000 Female Population

Year	Center location; approximate date screening began																		
																	Sweden		
	Toledo, Ohio; 1947	Olmstead County, Minn.; 1951*	Memphis & Shelby County, Tenn.; 1952	Connecticut; 1955	New York State; 1955	British Columbia; 1955	Ljubljana, Slovenia; 1956	Louisville, Kentucky; 1956*		Shanghai, China 1958**	Aberdeen City, Scotland; 1960		Manitoba; 1962	Saskatchewan; 1962	Alberta; 1962	Finland; Early 1960s	Blekinge; Mid-1960s	Östergotland; Mid-1960s	Jämtland; 1972
	Age >20	All ages	Age >19	All ages	All ages	Age >20	All ages	Age 20-49	Age 49	Age 20-54	Age 20-59	Age ≥60	Age 30-59	Age 35-64	Age 35-64	Age 25-60	Age >20	Age >20	Age >20
1937				20.8															
1940		15.3																	
1942				18.6															
1943					25.4														
1945					25.8														
1946														38					
1947				19.8	27.3									37					
1948														29					
1949			36		26.1									31					
1950	75		42											36					
1951	72	17.4	35		25.0						28.6	33.5		35					
1952	60		42	18.1										30					
1953	51		54		23.7		27.5							30	54				
1954	50		50				29.9	35.0	63.4					40	45				
1955	45		68		20.5	28.4	26.1							31	57				
1956	46		44			27.2	26.9							31	41				
1957	41		42	17.1	18.2	26.0	25.4	43.4	78.1					25	51	28.5			
1958	39		41			23.7	28.5			66.1				21	54	30.0			
1959	32		32		20.7	22.6	23.1			53.2				24	52	27.0			
1960	31		27			19.7	22.2	41.7	73.3	53.2				33	46	30.5			
1961	31		18		16.1	23.2	21.9			39.0	28.9	40.4		26	37	28.0	30	26	29
1962		9.4		13.6		15.5	29.1			76.3			38	26	43	34.5	28	27	29
1963					16.8	19.1	18.5	32.4	53.5	78.1			39	46	41	31.5	30	30	22
1964						16.3	18.1			80.2			38	35	39	29.0	28	40	27
1965						14.7	13.8			79.0			32	32	39	30.0	33	42	28
1966						13.6	14.5	20.2	44.0	71.0	21.8	24.5	43	35	36	27.0	30	39	29
1967				11.6		14.3	16.2			26.3			38	40	46	27.5	27	36	31
1968						13.0	15.4			32.0			27	20	37	25.0	18	31	29
1969						13.9	15.3			26.8			36	25	37	24.0	14	29	29
1970						12.3	11.9			18.1			30	19	26	20.0	11	19	25
1971						10.6	13.4			18.5			25	19	32		11	19	25
1972				10.9		9.2	14.2			23.8			17	18	34				
1973						9.5							22	11	25				
1974						8.6													
1975						8.7													

*Olmstead rates are for ten-year or twelve-years periods, Connecticut rates for five-year periods, and Louisville rates for three-year periods. These data are shown at their midpoints.
**Rates include in-situ as well as invasive cervical cancer.
Sources: References 10, 27, 31, 39, 40, 48-56.

Source : Guzick (1978)

Trends in Mortality from Cervical Cancer per 100,000 Female Population

Year	Center location; approximate date screening began																		
	Olmstead County, Minn., 1951*	Memphis & Shelby County, Tenn.; 1952	California; Early 1950s			Connecticut; 1955*	New York State; 1955	British Columbia; 1955	Ljubljana, Slovenia; 1956	Louisville, Kentucky 1956			Aberdeen City, Scotland; 1960		Finland; Early 1960s	England and Wales; 1964			Fredericksburg, Copenhagen; 1962
	All ages	Age >19	All ages	Age 25–34	Age 65–74	All ages	All ages	Age >20	All ages	Age 20-44	Age 45-64	Age >64	Age 20-59	Age >59	Age 25-59	Age 20-44	Age 45-64	Age >64	Age 30-54
1937	4.8					7.4													
1942	5.2					7.4													
1943							14.6												
1945							15.0												
1947	6.5					7.1	13.4												
1949							13.3												
1950			10.7	3.8	28.1														
1951		16					12.2												
1952	6.6	14				6.4													
1953		22					10.5		10.9										
1954		18							12.6										
1955		13					10.2		11.3	5.2	41.7	32.0				3.7	19.7	31.3	
1956		16							7.5	8.4	36.5	23.6				3.8	19.4	31.9	21
1957	7.0	19				5.9	9.1		10.9	5.1	32.1	47.7				4.2	18.1	30.8	
1958		13						11.4	10.3	5.3	37.8	32.1				4.4	20.7	31.7	
1959		13					9.9	10.6	14.6	10.9	40.2	38.2				4.4	18.2	31.3	
1960		16	8.8	2.0	28.8			9.9	13.3	7.7	32.4	25.6				4.7	18.7	30.1	
1961		9					7.8	10.3	12.2	5.1	31.9	35.8	18.4	33.8		3.9	18.9	27.9	
1962	3.3					4.4		12.9	10.7	5.2	25.2	36.8				4.1	18.5	28.3	
1963							7.7	11.0	12.6	7.6	19.7	41.5			7.4	3.9	18.4	27.6	
1964			7.4	2.2	22.3			10.6	14.0	2.5	14.8	29.8			7.2	4.1	19.7	27.7	
1965								7.7	9.7	4.2	27.9	50.5			6.2	4.4	19.4	23.6	
1966	3.4							7.8	4.5	3.3	22.7	46.5			6.3	3.5	18.4	27.2	21
1967						4.1		6.4	8.8	1.9	18.3	23.0			6.4	3.2	19.4	25.1	
1968			5.5	1.6	20.3			8.8	6.8	4.2	24.1	13.0			5.5	3.1	20.1	23.7	
1969								7.1	5.8	2.5	18.4	28.0			6.2	2.9	18.8	25.0	
1970								6.9	6.2	2.5	17.5	22.3			5.6	2.6	19.1	23.4	
1971								8.0	3.7	4.1	17.2	24.4	10.1	27.9	6.0	2.8	19.1	22.4	
1972						2.6		6.0	8.2										9
1973								5.6											
1974								4.8											
1975								5.2											

*Olmstead and Connecticut rates are for three-year or five-year periods and are shown at their midpoints.
Sources: References 21, 27, 39, 51-60.

Source : Guzick (1978)

TABLE II.15

NUMBER OF CASES OF INVASIVE CERVICAL CANCER OBSERVED IN 1978,

AND THE NUMBER THAT MIGHT HAVE BEEN EXPECTED IN THE ABSENCE OF SCREENING

AGE	OBSERVED	'EXPECTED'	PROPORTION 'PREVENTED'	NUMBER 'PREVENTED'
20-24	45	57	0.21	12
25-29	163	241	0.32	78
30-34	282	438	0.36	156
35-39	281	458	0.39	177
40-44	233	393	0.41	160
45-49	292	441	0.34	149
50-54	399	553	0.28	154
55-59	549	673	0.18	124
60-64	454	518	0.12	64
65-69	441	474	0.07	33
70-74	290	306	0.05	16
75-79	213	222	0.04	9
80+	229	238	0.04	9
TOTAL	3871	5012	0.23	1141

TABLE IV.1

1961 CENSUS : FEMALES BY AGE/MARITAL STATE

THOUSANDS

Age	S	M	FM	Age	S	M	FM
0	376.7	0	0	51.	37.8	253.3	29.0
1	358.3	0	0	52	40.7	261.6	33.0
2	354.2	0	0	53	41.4	250.5	35.3
3	345.7	0	0	54	42.1	241.6	37.5
4	331.3	0	0	55	41.7	228.8	39.6
5	320.0	0	0	56	43.1	225.1	43.7
6	314.4	0	0	57	42.3	214.7	46.6
7	322.3	0	0	58	41.9	209.5	51.2
8	316.4	0	0	59	41.3	198.5	54.6
9	316.6	0	0	60	42.0	195.5	63.2
10	324.2	0	0	61	38.9	174.1	63.3
11	338.7	0	0	62	38.8	162.3	65.7
12	353.0	0	0	63	38.5	154.2	69.5
13	389.7	0	0	64	37.4	144.1	74.1
14	411.1	0	0	65	37.8	134.8	78.0
15	316.1	0	0	66	35.6	122.7	78.9
16	331.4	2.8	0	67	35.5	113.2	82.2
17	313.2	11.5	0	68	34.9	106.2	86.0
18	285.6	30.7	0	69	32.8	94.5	86.3
19	228.1	58.6	0.1	70	32.7	87.1	91.6
20	180.2	95.5	0.1	71	29.3	73.6	84.8
21	150.4	143.3	0.3	72	29.5	70.0	92.4
22	116.0	178.4	0.6	73	28.0	61.5	91.8
23	89.8	201.9	0.9	74	26.2	53.1	90.3
24	70.5	214.5	1.2	75	24.6	46.2	89.0
25	57.2	225.0	1.6	76	23.3	40.4	87.1
26	47.8	228.9	2.1	77	20.6	32.8	79.3
27	40.8	229.2	2.3	78	19.4	27.8	77.5
28	38.2	238.5	2.7	79	17.7	22.8	71.6
29	35.8	247.1	3.1	80	17.0	19.3	70.4
30	36.4	262.6	3.8	81	14.1	14.5	59.3
31	32.3	255.1	4.0	82	12.5	11.5	54.3
32	31.8	258.6	4.4	83	10.9	8.8	48.2
33	30.2	254.9	4.9	84	9.8	6.7	43.0
34	31.6	266.6	5.5	85	8.1	4.7	36.0
35	32.1	275.7	6.7	86	6.6	3.6	30.5
36	30.8	273.4	7.3	87	5.2	2.3	23.4
37	31.0	278.2	8.4	88	4.2	1.6	18.8
38	31.8	288.3	9.8	89	3.3	1.0	14.2
39	33.4	307.2	11.6	90	2.6	.7	11.2
40	36.4	330.3	14.1	91	1.8	.4	7.9
41	31.7	302.0	14.1	92	1.3	.3	5.9
42	25.8	229.3	12.1	93	1.0	.2	4.1
43	25.7	217.3	12.4	94	.7	.1	3.0
44	29.8	246.3	15.4	95	.5	.1	2.0
45	31.8	259.0	17.4	96	.3	.1	1.4
46	34.4	282.1	21.0	97	.2	0	0.8
47	34.6	278.2	22.2	98	.2	0	0.6
48	35.9	275.3	24.0	99	.1	0	0.4
49	36.3	267.3	25.0	100	0	0	0.2
50	39.5	273.3	29.0				

Census 1961 (England and Wales) : Age, Marital Condition & General Tables (General Register Office 1964 H.M.S.O.).

TABLE IV.2

PARITY OF WOMEN BY MARITAL STATUS AND AGE

1979

Unpublished Table PSD 1. 51 from GHS 1979

ENGLAND & WALES

LIVEBORN CHILDREN

AGE		SINGLE	MARRIED	W.D.S.
16-17		0	5	0
	0	-	2 (40.0)	-
Para	1	-	3 (60.0)	-
	2	-	0	-
	3+	-	0	-
18-19		289	48	5
	0	279 (96.5)	26 (54.2)	0 (0.0)
Para	1	10 (3.5)	19 (39.6)	5 (100)
	2	0 (0.0)	3 (6.2)	0 (0.0)
	3+	0 (0.0)	0 (0.0)	0 (0.0)
20-24		341	498	31
	0	318 (93.3)	217 (43.6)	13 (41.9)
Para	1	19 (5.6)	161 (32.3)	12 (38.7)
	2	4 (1.2)	97 (19.5)	3 (9.7)
	3+	0 (0.0)	23 (4.6)	3 (9.7)
25-29		119	714	65
	0	104 (87.4)	180 (25.2)	16 (24.6)
Para	1	12 (10.1)	203 (28.4)	15 (23.1)
	2	2 (1.7)	255 (35.7)	24 (36.9)
	3+	1 (0.8)	76 (10.7)	10 (15.4)
30-34		64	895	79
	0	55 (85.9)	94 (10.5)	9 (11.4)
Para	1	6 (9.4)	171 (19.1)	26 (32.9)
	2	3 (4.7)	400 (44.7)	28 (35.4)
	3+	0 (0.0)	230 (25.7)	16 (20.3)
35-39		38	708	77
	0	27 (71.1)	60 (8.5)	4 (5.2)
Para	1	5 (13.2)	101 (14.3)	10 (13.0)
	2	2 (5.3)	276 (39.0)	33 (42.9)
	3+	4 (10.5)	271 (38.3)	30 (38.9)
40-44		31	682	72
	0	28 (90.3)	63 (9.2)	2 (2.8)
Para	1	2 (6.5)	62 (9.1)	11 (15.3)
	2	1 (3.2)	259 (38.0)	17 (23.6)
	3+	0 (0.0)	298 (43.7)	42 (58.3)
45-49		25	591	60
	0	23 (92.0)	51 (8.6)	12 (20.0)
Para	1	1 (4.0)	89 (15.1)	7 (11.7)
	2	0 (0.0)	203 (34.3)	15 (25.0)
	3+	1 (4.0)	248 (42.0)	26 (43.3)
ALL		907	4141	389
	0	834 (92.0)	693 (16.7)	56 (14.4)
Para	1	55 (6.1)	809 (19.5)	86 (22.1)
	2	12 (1.3)	1493 (36.1)	120 (30.8)
	3+	6 (0.6)	1146 (27.7)	127 (32.6)

ABLE IV.3

PARITY DISTRIBUTIONS OF STARTING POPULATION

Age	Single			Married			Form. married		
	Parity								
	0	1	2+	0	1	2+	0	1	2+
1	1000	0	0	1000	0	0	1000	0	0
2	1000	0	0	1000	0	0	1000	0	0
3	1000	0	0	1000	0	0	1000	0	0
4	1000	0	0	1000	0	0	1000	0	0
5	1000	0	0	1000	0	0	1000	0	0
6	1000	0	0	1000	0	0	1000	0	0
7	1000	0	0	1000	0	0	1000	0	0
8	1000	0	0	1000	0	0	1000	0	0
9	1000	0	0	1000	0	0	1000	0	0
10	1000	0	0	1000	0	0	1000	0	0
11	1000	0	0	1000	0	0	1000	0	0
12	1000	0	0	1000	0	0	1000	0	0
13	1000	0	0	1000	0	0	1000	0	0
14	1000	0	0	1000	0	0	1000	0	0
15	1000	0	0	1000	0	0	1000	0	0
16	990	10	0	1000	0	0	1000	0	0
17	990	10	0	667	333	0	1000	0	0
18	990	10	0	571	410	19	1000	0	0
19	980	20	0	564	396	40	1000	0	0
20	970	30	0	560	370	70	1000	0	0
21	970	30	0	538	356	106	500	500	0
22	970	30	0	514	347	139	333	333	334
23	970	30	0	462	356	182	400	400	200
24	970	30	0	408	359	233	250	500	250
25	960	40	0	358	354	288	333	417	250
26	950	50	0	309	343	348	344	375	281
27	920	70	10	266	329	405	316	368	316
28	920	70	10	239	326	435	273	364	363
29	920	70	10	204	297	499	269	346	385
30	910	80	10	184	281	535	276	345	379
31	920	70	10	167	267	566	250	333	417
32	910	80	10	155	257	588	237	329	434
33	900	90	10	146	249	605	238	333	429
34	890	100	10	142	243	615	234	319	447
35	890	100	10	138	242	620	226	321	453
36	890	100	10	133	241	626	222	317	461
37	890	100	10	131	240	629	200	343	457
38	890	100	10	128	241	631	213	312	475
39	890	100	10	127	243	630	213	319	468
40	890	100	10	125	244	631	196	330	474
41	890	100	10	126	248	626	199	331	470
42	890	100	10	125	247	628	191	324	485
43	890	100	10	128	247	625	197	308	495
44	890	100	10	132	250	618	185	311	504
45	890	100	10	139	255	606	196	304	500
46	890	100	10	143	254	603	192	299	509
47	890	100	10	145	255	600	182	291	527
48	890	100	10	155	259	586	186	288	526
49	890	100	10	162	263	575	198	289	513
50	890	100	10	169	264	567	192	282	526
51	890	100	10	196	271	533	203	273	524
52	890	100	10	196	271	533	203	273	524
53	890	100	10	196	271	533	203	273	524
54	890	100	10	196	271	533	203	273	524
55	890	100	10	196	271	533	203	273	524
56	890	100	10	229	266	505	215	258	527
57	890	100	10	229	266	505	215	258	527
58	890	100	10	229	266	505	215	258	527
59	890	100	10	229	266	505	215	258	527
60	890	100	10	229	266	505	215	258	527

Age	Single			Married			Form. married		
	Parity								
	0	1	2+	0	1	2+	0	1	2+
61	890	100	10	239	234	417	205	236	559
62	890	100	10	239	234	417	205	236	559
63	890	100	10	239	234	417	205	236	559
64	890	100	10	239	234	417	205	236	559
65	890	100	10	239	234	417	205	236	559
66	890	100	10	233	234	543	190	216	594
67	890	100	10	233	234	543	190	216	594
68	890	100	10	233	234	543	190	216	594
69	890	100	10	233	234	543	190	216	594
70	890	100	10	233	234	543	190	216	594
71	890	100	10	227	204	569	178	199	623
72	890	100	10	227	204	569	178	199	623
73	890	100	10	227	204	569	178	199	623
74	890	100	10	227	204	569	178	199	623
75	890	100	10	227	204	569	178	199	623
76	890	100	10	217	189	594	164	180	656
77	890	100	10	217	189	594	164	180	656
78	890	100	10	217	189	594	164	180	656
79	890	100	10	217	189	594	164	180	656
80	890	100	10	217	189	594	164	180	656
81	890	100	10	210	174	616	151	159	690
82	890	100	10	210	174	616	151	159	690
83	890	100	10	210	174	616	151	159	690
84	890	100	10	210	174	616	151	159	690
85	890	100	10	210	174	616	151	159	690
86	890	100	10	210	174	616	151	159	690
87	890	100	10	210	174	616	151	159	690
88	890	100	10	210	174	616	151	159	690
89	890	100	10	210	174	616	151	159	690
90	890	100	10	210	174	616	151	159	690
91	890	100	10	210	174	616	151	159	690
92	890	100	10	210	174	616	151	159	690
93	890	100	10	210	174	616	151	159	690
94	890	100	10	210	174	616	151	159	690
95	890	100	10	210	174	616	151	159	690
96	890	100	10	210	174	616	151	159	690
97	890	100	10	210	174	616	151	159	690
98	890	100	10	210	174	616	151	159	690
99	890	100	10	210	174	616	151	159	690
00	890	100	10	210	174	616	151	159	690

Source

Married/formerly married:

Census 1961 (E & W) Fertility Tables
GRO 1966 (HMSO)

Single:

Estimates based on data from GHS 1979
+ Werner (1982)

TABLE IV.4

LIFE TABLE DEATH RATES (FEMALE) 1970–72

Age	q_x	Age	q_x
0	.01523	51	.00489
1	.00106	52	.00531
2	.00067	53	.00576
3	.00052	54	.00624
4	.00041	55	.00676
5	.00034	56	.00733
6	.00030	57	.00795
7	.00028	58	.00864
8	.00026	59	.00941
9	.00024	60	.01025
10	.00023	61	.01120
11	.00022	62	.01227
12	.00021	63	.01348
13	.00022	64	.01486
14	.00025	65	.01641
15	.00039	66	.01818
16	.00035	67	.02017
17	.00039	68	.02243
18	.00043	69	.02498
19	.00045	70	.02784
20	.00045	71	.03104
21	.00045	72	.03462
22	.00044	73	.03860
23	.00044	74	.04301
24	.00044	75	.04787
25	.00045	76	.05323
26	.00047	77	.05910
27	.00049	78	.06550
28	.00052	79	.07250
29	.00056	80	.08014
30	.00060	81	.08846
31	.00065	82	.09752
32	.00070	83	.10734
33	.00077	84	.11795
34	.00084	85	.12937
35	.00093	86	.14157
36	.00103	87	.15456
37	.00114	88	.16831
38	.00128	89	.18281
39	.00143	90	.19805
40	.00160	91	.21413
41	.00180	92	.23113
42	.00202	93	.24912
43	.00226	94	.26817
44	.00253	95	.28831
45	.00281	96	.30954
46	.00311	97	.33186
47	.00343	98	.35523
48	.00377	99	.37957
49	.00412	100	.40489
50	.00449		

1. Source:
Life Tables 1970–1972. OPCS Monitor D.S. No.2 (1979)

2. Figures represent q_x values i.e.
Proportion of those attaining exact age x who die in ensuing year.

TABLE IV.5

RATES OF MARRIAGE, REMARRIAGE & WIDOWHOOD/DIVORCE

1961 - 1970

(rates per 1000)

AGE	S→M	M→FM*	FM→M
16	20	)	-
17	50	) 1	-
18	104	)	-
19	169	)	-
20	222	)	)
21	298	)	)
22	287	) 5	) 458
23	266	)	)
24	234	)	)
25	203	)	)
26	173	)	)
27	149	) 8	) 357
28	129	)	)
29	112	)	)
30-34	73	7	214
35-39	38	7	120
40-44	21	8	74
45-49	14	10	40
50-54	8	14	27
55-59	)	21	)
60-64	)	32	)
65-69	)	47	)
70-74	) 2	66	) 3
75-79	)	)	)
80-84	)	) 106	)
85 +	)	)	)

* Includes divorces based only on 1964-67 rates

Source

Marriage and Divorce Statistics 1974. OPCS Monitor FM2 no 1 (HMSO, 1977)

RATES OF MARRIAGE, REMARRIAGE & WIDOWHOOD/DIVORCE

1971-1980

(rates per 1000)

AGE	S→M	M→FM	FM→M
16	14	)	-
17	43	) 2	-
18	106	)	-
19	149	)	-
20	182	)	)
21	213	)	)
22	227	) 17	) 509
23	215	)	)
24	198	)	)
25	170	)	)
26	162	)	)
27	147	) 21	) 310
28	131	)	)
29	117	)	)
30-34	84	18	201
35-39	42	15	)
40-44	23	14	) 114
45-49	15	14	)
50-54	10	16	) 45
55-59	)	23	)
60-64	)	31	)
65-69	)	45	)
70-74	) 2	66	) 4
75-79	)	93	)
80-84	)	121	)
85+	)	165	)

Source

Marriage and Divorce Statistics 1980. OPCS MONITOR FM2 no 7 (HMSO 1981)

TRANSITION RATES BETWEEN MARITAL STATES

Figures represent probability of transfer per 1000 attaining exact age between 1 and 100

000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 020 050 104 169 222 298 287 266 234 203 173 149 129 112 094 081 073 062 055 049 043 038 033 029 026 023 021 019 017 016 015 014 013 012 011 010 009 008 007 006 005 005 005 004 003 002 002 002 002 002 002 002 002 002 002 002 002 002 001 001 001 001 001 001 001 001 001 001 001 001 001 000 000 000 000 000 000 000 000 000 000 000 000 000	S⟶M	1961-1970
000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 001 002 003 004 005 005 006 006 007 007 008 008 008 007 007 007 007 007 007 007 007 007 007 008 008 008 008 009 009 010 010 011 011 012 013 014 015 016 017 019 021 023 025 027 029 032 035 038 041 044 047 050 054 058 062 066 070 074 079 084 090 096 103 110 117 125 131 136 141 146 150 154 158 162 166 170 174 178 182 186 190 194 198	M⟶FM	
000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 580 559 539 519 498 478 458 438 418 397 377 357 327 298 270 242 214 187 165 148 132 120 108 098 090 082 074 066 058 051 045 040 036 033 031 029 027 025 023 021 019 017 015 014 013 012 011 010 009 008 007 006 005 005 004 004 004 003 003 003 003 002 002 002 002 002 001 001 001 001 001 001 000 000 000 000 000 000 000 000 000 000 000 000	FM⟶M	
000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 014 043 106 149 182 213 227 215 198 170 162 147 131 117 106 094 084 076 065 058 050 042 038 034 030 026 023 021 020 018 017 015 014 013 012 011 010 009 009 008 008 007 007 006 006 005 005 004 004 003 003 002 002 001 001 001 001 001 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000	S⟶M	1971-1980
000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 001 002 004 007 010 013 017 018 019 020 021 021 020 020 019 019 018 018 017 017 016 015 015 015 014 014 014 014 014 014 014 014 014 014 014 015 016 017 018 019 021 023 024 026 027 029 031 033 035 038 041 045 048 052 056 061 066 071 076 081 087 093 098 103 109 115 121 128 136 145 155 165 175 195 215 225 255 295 335 385 445 515 595 700	M⟶FM	
000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 770 720 680 640 592 544 508 455 410 376 344 310 290 267 244 222 200 178 158 140 125 114 097 084 070 056 045 037 030 024 020 019 018 017 016 015 014 013 013 012 012 011 011 010 010 009 009 008 008 007 007 006 006 005 005 004 004 003 003 002 002 001 001 001 001 001 001 001 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000	FM⟶M	
000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 018 046 105 159 181 211 229 207 187 174 161 144 132 123 107 095 084 072 062 056 048 042 037 033 030 026 023 021 019 017 016 015 013 012 011 010 009 008 007 006 005 004 003 002 002 002 002 002 002 002 002 002 002 002 002 002 002 001 001 001 001 001 001 001 001 001 001 001 001 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000	S⟶M	1981-1990
000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 001 002 004 008 012 017 018 019 020 021 021 020 020 019 019 018 018 017 017 016 016 016 015 015 014 014 014 014 014 015 015 015 016 016 016 017 017 018 019 020 021 023 025 027 029 031 033 036 039 042 045 049 053 057 061 066 071 077 081 087 093 099 105 112 119 127 134 141 148 155 161 167 173 179 184 189 193 197 200 200 200 200 200	M⟶FM	
000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 740 720 700 670 640 600 544 480 430 380 338 302 280 255 234 215 198 186 175 161 150 139 129 120 114 104 092 084 076 070 064 057 052 048 045 042 039 036 033 030 027 024 021 018 015 012 009 006 004 004 004 004 004 003 003 003 003 003 002 002 002 002 002 001 001 001 001 001 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000 000	FM⟶M	

TABLE IV.1

FERTILITY RATES : MARRIED WOMEN 1961-1970

1. AVERAGE ANNUAL BIRTHS BY AGE/PARITY 1961-70

AGE	PARA 0	PARA 1	PARA 2 +
16-19	47,320	10,450	1,080
20-24	135,660	86,370	35,470
25-29	69,880	91,040	79,560
30-34	21,680	38,750	70,970
35-39	7,260	12,870	42,580
40-49	1,610	2570	14,150

Source : Registrar Generals Review of England and Wales, Part II, Population - 1961 - 1970 (Table HH)

2. MEAN POPULATION (ENGLAND & WALES 1966) BY AGE/PARITY

AGE	PARA 0	PARA 1	PARA 2 +
16-19	74,050	60,390	9350
20-24	389,250	315,980	210,660
25-29	257,250	341,000	598,250
30-34	148,230	259,400	827,630
35-39	143,900	261,650	902,680
40-49	336,650	646,400	1,710,200

Sources : Population : Census 1966 : Summary Tables
Parity : Census 1961 & 1971 : fertility Tables

3. MEAN AGE-PARITY SPECIFIC FERTILITY RATES (BIRTHS PER 1000 WOMEN)

AGE	PARA 0	PARA 1	PARA 2 +
16-19	640	174	115
20-24	348	273	168
25-29	272	267	133
30-34	146	150	86
35-39	50	49	47
40-49	5	4	8
% Females births	48%	49%	48%

FERTILITY RATES : MARRIED WOMEN 1971-1980

1. AVERAGE ANNUAL BIRTHS BY AGE/PARITY 1971-80

AGE	PARA 0	PARA 1	PARA 2 +
16-19	35,370	7,920	590
20-24	99,540	60,650	20,830
25-29	79,450	90,720	47,470
30-34	21,400	36,930	39,760
35-39	4,470	7,130	17,810
40-49	860	1,210	5,310

Source : Birth Statistics, Series FM1 nos 1-7 (Tables 4.1, 4.2)

2. MEAN POPULATION (ENGLAND & WALES 1976) BY AGE/PARITY

AGE	PARA 0	PARA 1	PARA 2 +
16-19	65,000	58,400	1800
20-24	463,300	285,500	187,200
25-29	393,500	389,000	731,100
30-34	191,300	240,800	943,900
35-39	138,900	184,400	906,200
40-49	297,700	372,700	1,749,900

Sources : Population estimates by marital status : Marriage and Divorce Statistics 1976, FM 2 no 3.
Parity of married women : GHS data for 1975-77 (unpublished tables : GRO 51)

3. MEAN AGE-PARITY SPECIFIC FERTILITY RATES (BIRTHS PER 1000 WOMEN)

AGE	PARA 0	PARA 1	PARA 2 +
16-19	544	136	(325)
20-24	215	240	111
25-29	202	233	65
30-34	112	153	42
35-39	32	39	20
40-49	3	3	3
% Female Births	48%	49%	48%

FERTILITY RATES : UNMARRIED FEMALES

Figures are all Illegitimate Live Births (both sexes)
Per 1000 Single, Widowed and Divorced Women

AGE	PERIOD 1961-70	1971-80
15-19	12	13
20-24	30	26
25-29	50	35
30-34	42	30
35-39	24	16
40-44	7	4
45-49	1	0

Source : Birth Statistics (1980). OPCS Monitor FM1 No. 7 (HMSO 1982)

HYSTERECTOMY PROBABILITIES

1966 & 1976

Data sources :

1. Annual number of total hysterectomies (not for cancer) : HIPE
2. Population at risk : 1966 census, 1976 estimates
3. Prevalence of hysterectomy by age : estimates from Alderson & Donnan (1978)

	1966				1976			
AGE	Total no. of hysterectomies (not cancer) of cervix	Pop. (1000)	Pop. with uterus	Prob. of hysterectomy (per 1000)	Total no. of hysterectomies (not cancer) of cervix	Pop. (1000)	Pop. with uterus	Prob. of hysterectomy (per 1000)
15-19	30	1629	1629	0.02	10	1699	1699	0.01
20-24	160	1639	1639	0.10	110	1648	1648	0.07
25-29	460	1473	1472	0.31	1650	1841	1841	0.90
30-34	2190	1416	1411	1.55	4910	1570	1556	3.16
35-39	5560	1473	1451	3.83	8940	1395	1359	6.58
40-44	10350	1598	1538	6.73	11490	1358	1285	8.94
45-49	10910	1535	1445	7.55	10980	1441	1313	8.36
50-54	6010	1610	1502	4.00	5970	1537	1382	4.32
55-59	2380	1589	1490	1.60	2280	1446	1310	1.74
60-64	2150	1459	1371	1.57	2170	1461	1349	1.61
65-69	1360	1241	1165	1.17	2360	1391	1292	1.83
70-74	1000	1004	943	1.06	1880	1173	1089	1.73
75-79	580	726	682	0.85	940	826	767	1.22
80-84	180	457	429	0.42	320	526	488	0.66
85+	50	271	245	0.20	160	393	365	0.44

HYSTERECTOMY : ESTIMATED PREVALENCE IN 1961

AGE	per 1000 PREVALENCE
30-34	1.5
35-39	10
40-44	25
45-49	42
50-54	50.5
55-59	52.5
60-64	53
65-69	54
70-74	(54.5)
75-79	(55)
80+	(55)

Source: From data of Alderson & Donnan (1978)
Figures in parenthesis are extrapolations

TABLE IV.13

PREVALENCE OF STATES 2-5

(PER 10,000)

AGE GROUP	STATE 2	3	4	5
0 - 4	0	0	0	0
5 - 9	0	0	0	0
10-14	0	0	0	0
15-19	40	3	0	0
20-24	120	18	0	0
25-29	147	49	1	1
30-34	130	76	3	2
35-39	108	90	5	8
40-44	88	88	8	15
45-49	67	79	9	20
50-54	61	68	10	22
55-59	60	58	9	21
60-64	59	51	8	20
65-69	58	45	8	18
70-74	57	40	7	17
75-79	56	36	7	14
80-84	55	33	7	12
85-89	54	30	6	10
90-94	53	28	6	10
95-99	52	26	6	10

TABLE IV.15

INCIDENCE OF CLINICAL CERVIX CANCER

ANNUAL REGISTRATIONS PER 100,000 WOMEN

AGE	England & Wales 1962-1965	Four English Regions 1960-1962
20-24	0.6	0.2
25-29	2.5	1.8
30-34	7.8	7.8
35-39	22.0	21.8
40-44	37.0	31.6
45-49	39.4	31.9
50-54	37.3	31.1
55-59	34.0	30.4
60-64	32.4	31.1
65-69	30.6	31.0
70-74	32.0	30.5
75-79	29.6	31.9
80-84	29.0	30.6
85+	22.4	27.4
ALL AGES	18.0	16.9

Sources :

England & Wales : Registrar Generals Statistical Review of England & Wales for 1965. Supplement on Cancer (Table B) 1970 G.R.O.

Four English Regions : Doll et al (1966). Cancer Incidence in Five Continents Vol. I

TABLE IV.15

	Parity 0	Parity 1	Parity 2+
Single	84 56	88 89	94 96
Married	90 61	95 98	101 106
Formerly Married	145 138	158 220	168 238

Upper figures : Standard prevalence ratios (dysplasia - microinvasive) 1
Lower figures : Age-adjusted relative risk (dysplasia - microinvasive) 2

1 Parkin et al (1981) Public Health 96, 3 - 14
2 Parkin et al (1982) Brit. J. Obstet. Gynecol. 89

ABLE IV.16

TRANSITION RATES : DATA 11M

Columns								
1	2	3	4	5	6	7		
1	2	16	20	0	99	0.17	¦	
1	2	21	25	0	99	0.50	¦	
1	2	26	30	0	99	0.45	¦	
1	2	31	35	0	99	0.37	¦	Incidence of Dysplasia
1	2	36	40	0	99	0.31	¦	
1	2	41	45	0	99	0.25	¦	
1	2	46	50	0	99	0.19	¦	
1	2	51	100	0	99	0.12	¦	
2	1	16	50	0	99	25.00		
2	1	51	100	0	99	12.50		
2	3	16	100	0	99	5.0		
3	2	16	50	0	99	1.0		
3	2	51	100	0	99	0.5		
3	4	16	20	0	99	0.5	}	
3	4	21	25	0	99	1.0	}	
3	4	26	30	0	99	1.5	}	
3	4	31	35	0	99	2.0	}	
3	4	36	40	0	99	3.0	}	Conversion of CIS
3	4	41	50	0	99	5.0	}	(age dependant only)
3	4	51	60	0	99	7.0	}	
3	4	61	70	0	99	8.0	}	
3	4	71	80	0	99	9.0	}	
3	4	81	100	0	99	10.0	}	
4	5	16	100	1	1	0.0		
4	5	16	100	2	99	100.0		
5	8	16	30	1	1	10.0	]	
5	8	16	30	2	3	4.0	]	
5	8	16	30	4	5	2.0	]	
5	8	31	40	1	1	12.0	]	
5	8	31	40	2	3	5.0	]	
5	8	31	40	4	5	3.0	]	
5	8	41	50	1	1	18.0	]	
5	8	41	50	2	3	8.0	]	
5	8	41	50	4	5	4.0	]	
5	8	51	60	1	1	22.0	]	Survival rates
5	8	51	60	2	3	12.0	]	
5	8	51	60	4	5	5.0	]	
5	8	61	70	1	1	27.0	]	
5	8	61	70	2	3	14.0	]	
5	8	61	70	4	5	6.0	]	
5	8	71	80	1	1	41.0	]	
5	8	71	80	2	3	18.0	]	
5	8	71	80	4	5	6.0	]	
5	8	81	100	1	1	55.0	]	
5	8	81	100	2	3	20.0	]	
5	8	81	100	4	5	6.0		
5	8	16	100	6	99	2.0		

//

Columns

1 From state

2 To state

3) between ages
4)

5) duration in state in column 1
6)

7 Transfer rate, per 100

TABLE IV.17

TRANSITION RATES : DATA 11N

```
1  2  16 20 0 99    0.17  ¦
1  2  21 25 0 99    0.50  ¦
1  2  26 30 0 99    0.45  ¦
1  2  31 35 0 99    0.37  ¦  Incidence
1  2  36 40 0 99    0.31  ¦of Dysplasia
1  2  41 45 0 99    0.25  ¦
1  2  46 50 0 99    0.19  ¦
1  2  51100 0 99    0.12  ¦
2  1  16 50 0 99   25.00
2  1  51100 0 99   12.50
2  3  16 85 0  1    2.0    *c.i.s.
2  3  16 85 2 99   10.0    *rather
3  2  16 60 1 99    5.0    *transient
3  2  61100 1 99    2.5    *
3  4  16 20 0 99    0.5     }
3  4  21 25 0 99    1.0     }
3  4  26 30 0 99    1.5     }
3  4  31 35 0 99    2.0     }
3  4  36 40 0 99    3.0     }  Conversion of CIS
3  4  41 50 0 99    5.0     } (age dependant only)
3  4  51 60 0 99    7.0     }
3  4  61 70 0 99    8.0     }
3  4  71 80 0 99    9.0     }
3  4  81100 0 99   10.0     }
4  5  16100 1  1    0.0
4  5  16100 2 99  100.0
5  8  16 30 1  1   10.0     ]
5  8  16 30 2  3    4.0     ]
5  8  16 30 4  5    2.0     ]
5  8  31 40 1  1   12.0     ]
5  8  31 40 2  3    5.0     ]
5  8  31 40 4  5    3.0     ]
5  8  41 50 1  1   18.0     ]
5  8  41 50 2  3    8.0     ]
5  8  41 50 4  5    4.0     ]
5  8  51 60 1  1   22.0     ]  Survival rates
5  8  51 60 2  3   12.0     ]
5  8  51 60 4  5    5.0     ]
5  8  61 70 1  1   27.0     ]
5  8  61 70 2  3   14.0     ]
5  8  61 70 4  5    6.0     ]
5  8  71 80 1  1   41.0     ]
5  8  71 80 2  3   18.0     ]
5  8  71 80 4  5    6.0     ]
5  8  81100 1  1   55.0     ]
5  8  81100 2  3   20.0     ]
5  8  81100 4  5    6.0     ]
5  8  16100 6 99    2.0     ]
//
```

TABLE IV.18

TRANSITION RATES : DATA 110

```
1   2   16 20  0 99     0.17  |
1   2   21 25  0 99     0.50  |
1   2   26 30  0 99     0.45  |
1   2   31 35  0 99     0.37  |  Incidence
1   2   36 40  0 99     0.31  |of Dysplasia
1   2   41 45  0 99     0.25  |
1   2   46 50  0 99     0.19  |
1   2   51100 0 99     0.12  |
2   1   16 50  1 99    25.00
2   1   51100 1 99    12.50
2   3   16100 0  1     2.0   }
2   3   16100 2 99    10.0   }
3   2   16 50  1 99     5.0
3   2   51100 1 99     2.5
3   4   16 50  0  2     0.05  }
3   4   16 50  3  5     1.0   }
3   4   16 50  6  8     2.0   }
3   4   16 50  9 11     4.0   }   time dependant progression
3   4   16 5012 14     8.0   }    from states 2 and 3
3   4   16 5015 17    16.0   }
3   4   16 5018 99    32.0   }
3   4   51100 0  2     1.0   }
3   4   51100 3  5     2.0   }
3   4   51100 6  8     4.0   }
3   4   51100 9 11     8.0   }
3   4   5110012 14    16.0   }
3   4   5110015 99    32.0   }
4   5   16100 0  1     0.0
4   5   16100 2 99   100.0
5   8   16 30  1  1    10.0   ]
5   8   16 30  2  3     4.0   ]
5   8   16 30  4  5     2.0   ]
5   8   31 40  1  1    12.0   ]
5   8   31 40  2  3     5.0   ]
5   8   31 40  4  5     3.0   ]
5   8   41 50  1  1    18.0   ]
5   8   41 50  2  3     8.0   ]
5   8   41 50  4  5     4.0   ]
5   8   51 60  1  1    22.0   ]
5   8   51 60  2  3    12.0   ]  Survival rates
5   8   51 60  4  5     5.0   ]
5   8   61 70  1  1    27.0   ]
5   8   61 70  2  3    14.0   ]
5   8   61 70  4  5     6.0   ]
5   8   71 80  1  1    41.0   ]
5   8   71 80  2  3    18.0   ]
5   8   71 80  4  5     6.0   ]
5   8   81100  1  1    55.0   ]
5   8   81100  2  3    20.0   ]
5   8   81100  4  5     6.0   ]
5   8    16100 6 99     2.0   ]
//
```

TABLE V.I

POPULATION SIZE

	OBSERVED (E & W)		SIMULATED
	Pop. (numbers)	% start	
1961	23,801	100	100
1971	25,067	105.3	105.8
1981	25,474	107.0	105.4
1991	25,764	108.2	106.3

Sources:

GRO : Census 1961 Age, marital conditions and general tables. 1964 HMSO
OPCS : Census 1971 " " " " " 1974 HMSO
OPCS : Population trends vol. 1983 HMSO
OPCS : Population projections PP2 no 11 1981 HMSO

ABLE V.2

MORTALITY , FERTILITY

YEAR	BIRTH RATE (FEMALES PER 1000F)		DEATH RATE (FEMALES PER 1000F)	
	OBSERVED	SIMULATED	OBSERVED	SIMULATED
1961	16.5	16.7	11.4	9.6
1962	16.9	16.9	11.3	10.1
1963	17.2	15.6	11.6	10.3
1964	17.5	15.8	10.7	10.7
1965	17.2	16.1	10.9	9.9
1966	16.8	15.5	11.2	10.5
1967	16.3	16.4	10.7	10.8
1968	16.0	15.9	11.4	10.9
1969	15.5	16.4	11.3	11.1
1970	15.2	16.0	11.3	10.9
1971	15.1	11.7	11.1	11.8
1972	13.9	11.0	11.6	12.2
1973	13.0	11.2	11.5	11.4
1974	12.3	11.4	11.5	11.6
1975	11.6	11.1	11.4	11.7
1976	11.3	11.2	11.8	12.2
1977	11.0	11.6	11.4	12.3
1978	11.5	11.2	11.5	12.1
1979	12.3	12.0	11.7	12.0
1980		12.4	11.5	12.8
1981		13.0	11.3	12.9
1982		13.0		12.9

Sources: OPCS Monitors (Births; Mortality)
Population Trends (Population)

TABLE V.3

ESTIMATED PROPORTION OF WOMEN WITH HYSTERECTOMY, BY AGE-GROUP

(ENGLAND & WALES)

AGE	YEAR			
	1963	1968	1973	1978
25-29 :	0.000	0.001	0.002	0.003
30-34 :	0.002	0.005	0.009	0.013
35-39 :	0.013	0.017	0.026	0.033
40-44 :	0.030	0.045	0.054	0.064
45-49 :	0.049	0.068	0.089	0.096
50-54 :	0.056	0.078	0.101	0.122
55-59 :	0.056	0.069	0.094	0.117
60-64 :	0.056	0.064	0.077	0.101
65-69 :	0.058	0.064	0.071	0.084
70-74 :	0.058	0.066	0.072	0.080
75-79 :	0.055	0.064	0.071	0.078

Source: Parkin et al (1984)

TABLE V.4

COMPARISON OF 3 NATURAL HISTORIES

SCREENING POLICY: EXAMINATIONS AT AGES 35, 40, 45, 50, 55, 60, 65
ATTENDANCE RATE: 45% AND 80%, RANDOM
SENSITIVITY 70%, SPECIFICITY 99.5%
LOSS TO F.U.: 8% PA DYSPLASIA, 4% PA C.I.S. FOR 3 YEARS

OUTCOME 1961-1990

	11 M Attendance		11 N Attendance		11 O Attendance	
	80%	45%	80%	45%	80%	45%
% SAVINGS						
NEW CASES	57	45	54	40	64	46
DEATHS	53	41	49	41	55	37
LIFE-YEARS	56	42	48	41	56	37
TESTS						
TOTAL (Thousands)	193	109	192	109	192	109
% POSITIVE	1.7	1.8	1.6	1.8	1.8	1.9
- OF WHICH FALSE POS.	29.4	25.5	30.5	25.6	27.8	25.4
% SAVING PER 1000 TESTS						
CASES	0.30	0.41	0.28	0.37	0.33	0.42
DEATHS	0.27	0.38	0.26	0.38	0.29	0.34
LIFE-YEARS	0.29	0.38	0.25	0.38	0.29	0.34
% SAVING PER 1000 POS. TESTS						
CASES	17.6	22.9	17.5	20.1	18.8	22.0
DEATHS	16.4	21.1	15.8	20.7	16.2	17.4
LIFE-YEARS	17.3	21.4	15.5	20.6	16.4	17.6

TABLE V.5

EFFECT OF VARYING ATTENDANCE RATES

SCREENING POLICY: EXAMINATIONS AT AGES 35, 40, 45, 50, 55, 60, 65
ATTENDANCE: RANDOM, AT RATES SHOWN
SENSITIVITY 70%, SPECIFICITY 99.5%
LOSS TO F.U.: 8% PA DYSPLASIA, 4% PA CIS FOR 3 YEARS

NATURAL HISTORY: 11 M

OUTCOME 1961-1990

	ATTENDANCE RATE					
	15%	30%	45%	60%	75%	90%
SAVINGS						
CASES	166	246	340	399	435	469
DEATHS	85	120	170	195	221	226
LIFE-YEARS	1542	2451	3469	3725	4531	4818
TESTS						
TOTAL (Thousands)	36	72	109	144	180	216
POSITIVE	723	1292	1940	2364	3054	3526
- OF WHICH FALSE POS.	25%	28%	25%	28%	28%	30%
SAVINGS PER 1000 TESTS						
CASES	4.6	3.4	3.1	2.8	2.4	2.2
DEATHS	2.4	1.7	1.6	1.4	1.2	1.0
LIFE-YEARS	42.5	33.9	31.9	25.9	25.2	22.3
SAVINGS PER POSITIVE TEST						
CASES	0.23	0.19	0.18	0.17	0.14	0.13
DEATHS	0.12	0.09	0.09	0.08	0.07	0.06
LIFE-YEARS	2.13	1.90	1.79	1.58	1.48	1.37

TABLE V.6

EFFECT OF NON-RANDOM ATTENDANCE

SCREENING POLICY: EXAMINATIONS AT AGES 35, 40, 45, 50, 55, 60, 65
ATTENDANCE: AS SHOWN
SENSITIVITY: 70%, SPECIFICITY 99.5%
LOSS TO F.U.: 8% PA DYSPLASIA, 4% PA CIS FOR 3 YEARS

NATURAL HISTORY 11 M

OUTCOME 1961-1990

	ATTENDANCE AT SCREENING						
	OVERALL RATE ≥ 80%			OVERALL = 60%		OVERALL = 45%	
	Random	Attendance for normal state = X2 abnormal	Attendance ∝ marital state 5 : 9 : 2	Random	20% women never attend	Random	Attendance ∝ age 60% at 35 30% at 65
SAVINGS							
CASES	438	321	393	399	352	340	300
DEATHS	214	159	196	195	166	170	128
LIFE-YEARS	4442	3324	4021	3725	3167	3469	2751
TESTS							
TOTAL (Thousands)	193	192	190	144	145	109	110
POSITIVE	3230	2279	3172	2364	2421	1940	2049
- OF WHICH FALSE POS.	29%	42%	29%	28%	30%	25%	26%
SAVINGS PER 1000 TESTS							
CASES	2.3	1.7	2.1	2.8	2.4	3.1	2.7
DEATHS	1.1	0.8	1.0	1.4	1.1	1.6	1.2
LIFE-YEARS	23.1	17.4	21.2	25.9	21.8	31.9	25.1
SAVINGS PER POSITIVE TEST							
CASES	0.14	0.14	0.12	0.17	0.15	0.18	0.15
DEATHS	0.07	0.07	0.06	0.08	0.07	0.09	0.06
LIFE-YEARS	1.39	1.46	1.27	1.58	1.31	1.79	1.34

TABLE V.7

EFFECT OF TEST PARAMETERS & FOLLOW-UP INTENSITY

EXAMINATIONS AT AGES 35, 40, 45, 50, 55, 60, 65
ATTENDANCE: RANDOM, 80% PA

NATURAL HISTORY: 11 M

OUTCOME 1961-1990

% LOSS TO FOLLOW-UP (EACH YEAR FOR 3 YEARS)	0% DYSPLASIA 0% CIS	2% DYSPLASIA 1% CIS	8% DYSPLASIA 4% CIS		
TEST CHARACTERISTICS	70% SENSITIVITY 99.5% SPECIFICITY			90% SENSITIVITY 99% SPECIFICITY	50% SENSITIVITY 99.9% SPECIFICITY
SAVINGS					
CASES	455	442	438	521	373
DEATHS	230	223	214	269	163
LIFE-YEARS	4806	4533	4442	5390	3475
TESTS					
TOTAL (Thousands)	191	192	193	192	193
POSITIVE	3049	3106	3230	4704	1919
- OF WHICH FALSE POS.	31%	29%	29%	40%	10%
SAVINGS PER 1000 TESTS					
CASES	2.4	2.3	2.3	2.7	1.9
DEATHS	1.2	1.2	1.1	1.4	0.8
LIFE-YEARS	25.2	23.6	23.1	28.1	18.0
SAVINGS PER POSITIVE TEST					
CASES	0.15	0.14	0.14	0.11	0.19
DEATHS	0.08	0.07	0.07	0.06	0.08
LIFE-YEARS	1.58	1.46	1.39	1.15	1.81

TABLE V.8

COMPARISON OF SIMPLE SCREENING POLICIES

ATTENDANCE RATE: 80%
SENSITIVITY 70%, SPECIFICITY 99.5%
LOSS TO FOLLOW-UP: 85 PA DYSPLASIA, 4% PA C.I.S

NATURAL HISTORY 11 M

OUTCOME 1961-1990

SCREENING POLICY

	EXACT AGES 35, 40, 45, 50, 55, 60, 65			ALL WOMEN 35 - 65 FIVE-YEARLY	PREGNANCY ONLY
	ALL WOMEN	NOT PARA 0 NOT SINGLE	DYSPLASTIC TESTS IGNORED		
SAVINGS					
CASES	438	354	405	450	128
DEATHS	214	172	180	233	68
LIFE-YEARS	4442	3530	3360	4924	1969
TESTS					
TOTAL (Thousands)	193	153	194	194	89
POSITIVE	3230	2790	1871	3138	1444
- OF WHICH FALSE POS.	29%	29%	53%	30%	31%
PER 1000 TESTS					
CASES	2.2	2.3	2.1	2.3	1.4
DEATHS	1.1	1.1	0.9	1.2	0.8
LIFE-YEARS	23.1	23.1	17.3	25.4	22.0
SAVINGS PER POSTIVE TEST					
CASES	0.14	0.13	0.22	0.14	0.09
DEATHS	0.07	0.06	0.10	0.07	0.05
LIFE-YEARS	1.39	1.27	1.80	1.57	1.36

TABLE V.9

SCREENING POLICIES FOR ENGLAND AND WALES

1. Ministry of Health (1966)

Women over 35, five yearly intervals (? to 65).

2.

As above, but starting under age 35 after 3rd pregnancy.

3. British Society for Clinical Cytology (1977)

Start	:	25 for women attending for contraception, pregnancy or venereal disease.
		30 if sexually active and not already tested.
Intervals	:	Five yearly.
Stop	:	70 (no age limit for first test).

4.

As above, but 3 yearly intervals after age 35.

5. Committee on Gynaecological Cytology (1982)

(i) Early in each pregnancy.

(ii) Age 22 (or next visit): attenders at family planning - if not previously screened.

(iii) Age 30: attenders at family planning - if no smear in previous 5 years.

(iv) Anyone else age 25-35, sexually active, who requests a test.

(v) At exact ages 35, 40, 45, 50, 55, 60, 65.

(vi) Stop at 65 (if never had positive or doubtful smear).

(also, «diagnostic» tests considered «useful»).

TABLE V.10

COMPARISON OF POLICIES PROPOSED FOR ENGLAND & WALES

ATTENDANCE RATES: 80% (UNLESS STATED)
SENSITIVITY 70%, SPECIFICITY 99.5%
LOSS TO F.U.: 8% PA DYSPLASIA, 4% PA C.I.S.

NATURAL HISTORY: 11 M

OUTCOME 1961-1990

	POLICY				
	1 MOH	2 Modified MOH	3 BSCC[1]	4 BSCC[1] "Plus"	5 C.G.C.[2]
SAVINGS					
CASES	433	463	488	577	478
DEATHS	200	221	224	283	227
LIFE-YEARS	4081	4819	4852	6111	4858
TESTS					
TOTAL (THOUSANDS)	193	203	251	351	308
POSITIVE	3205	3366	4232	5210	4747
- OF WHICH FALSE POS.	29%	29%	30%	34%	31%
SAVINGS PER 1000 TESTS					
CASES	2.3	2.3	1.9	1.6	1.6
DEATHS	1.0	1.1	0.9	0.8	0.7
LIFE-YEARS	21.2	23.7	19.3	17.4	15.8
SAVINGS PER POSTIVE TEST					
CASES	0.14	0.14	0.12	0.11	0.10
DEATHS	0.06	0.07	0.05	0.05	0.05
LIFE-YEARS	1.27	1.43	1.15	1.17	1.02

[1] Between ages 25-29, annual probability of first test = 0.2 (normal), 0.4 (abnormal cervix)

[2] At 22 or 23) 50% annual probability of receiving first test
30) Prevalence of abnormality double in those attending

TABLE V.11

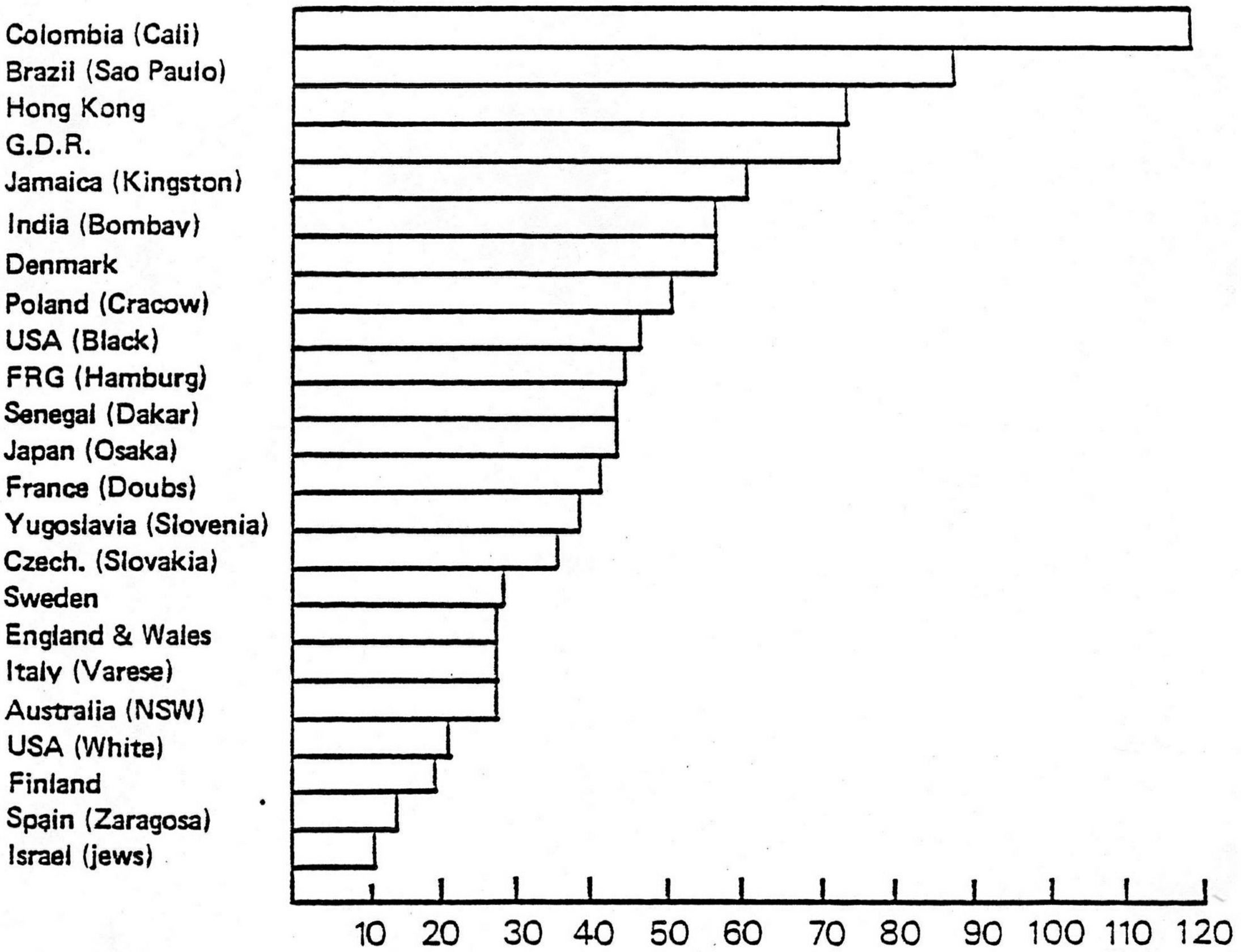
COST-EFFECTIVENESS OF POLICIES PROPOSED FOR ENGLAND & WALES

	POLICY				
COSTS	1 MOH	2 MOH +	3 BSCC	4 BSCC +	5 CGC
Negative tests (incidental): 0.5 per 1000	0	0	4.7	4.8	57
Negative tests (routine): 1.0 per 1000	190	200	238	336	189
False positive tests: 5.0 per 1000	4.7	4.9	6.3	8.8	7.3
True positive tests: 20.0 per 1000	45.2	47.6	59.6	69.0	65.6
Total cost	239.9	252.5	308.6	418.6	318.9
OUTPUT					
Life-years saved	4081	4819	4852	6111	4858
RATIO: Life-years per unit cost	17.0	19.1	15.7	14.6	15.2

Fig 2.1

Incidence of cervical carcinoma (age-standardised)

PER 100,000 aged 35-64



Source of data : USA : SEER (1981)
England and Wales : OPCS (1981)
Other : Waterhouse et al (1982)

Fig. 2.2

AGE-SPECIFIC INCIDENCE OF CARCINOMA OF CERVIX

Source : Doll et al (1966)

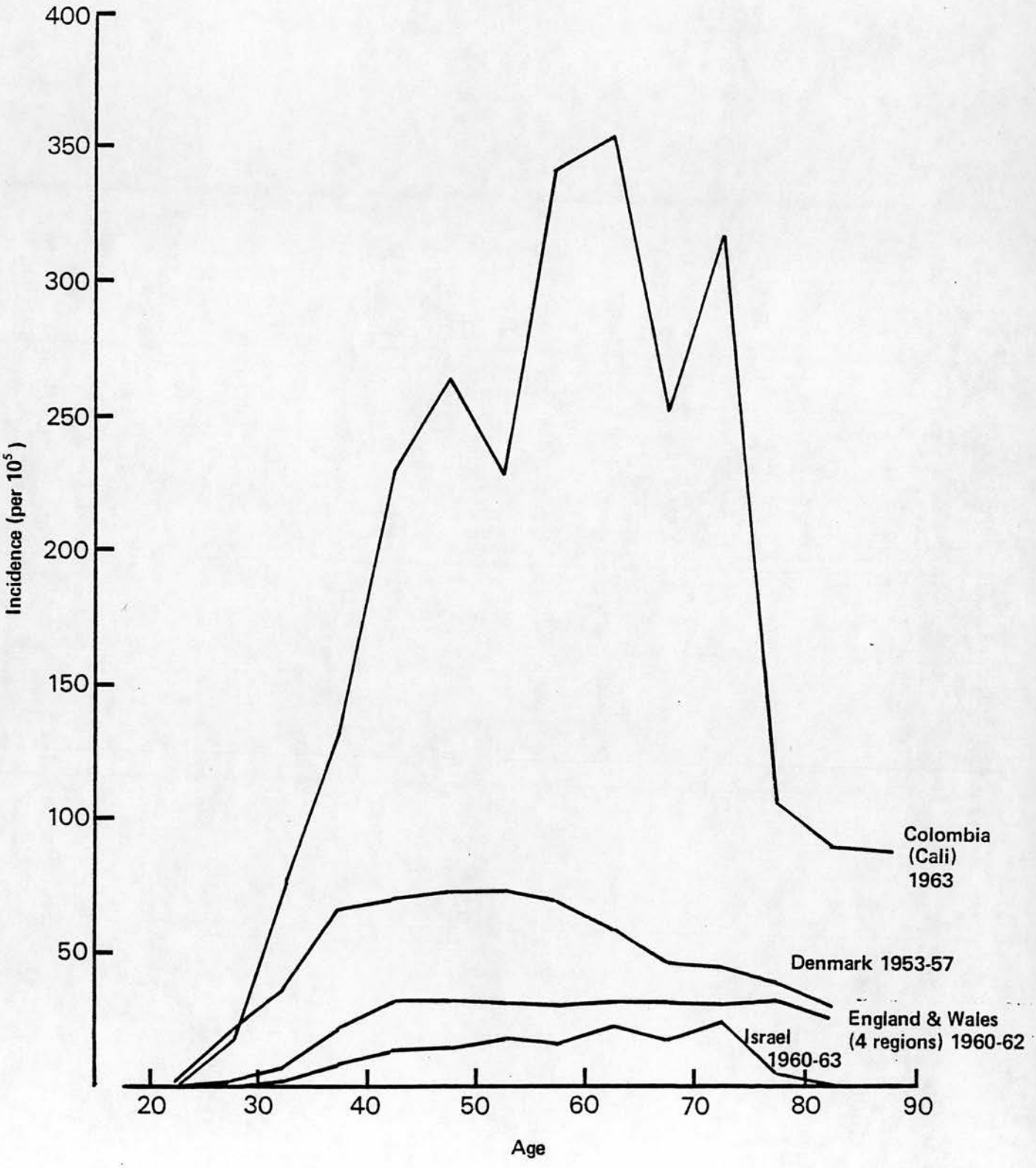
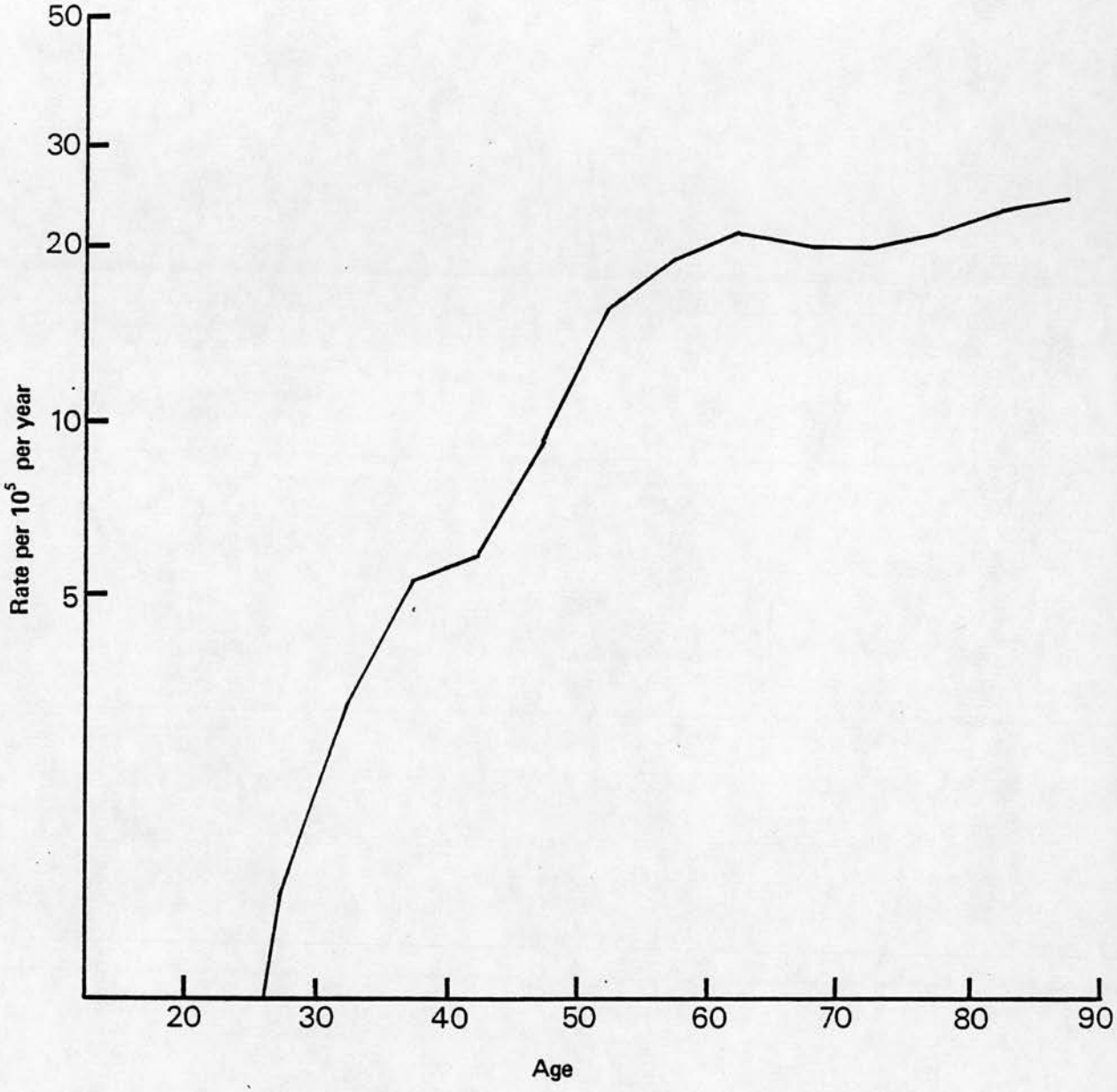


Fig. 2.3



MORTALITY FROM CARCINOMA OF CERVIX, ENGLAND & WALES 1976-1980

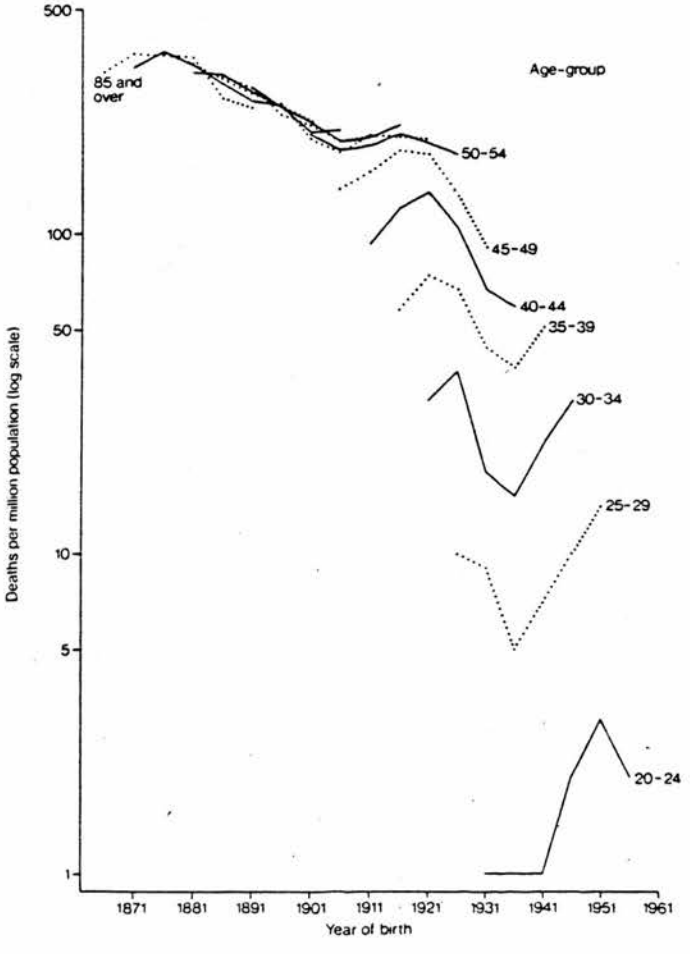
Source : Cancer mortality in England & Wales, 1976-1980, OPCS monitor DH1 82/2

Figure 2.4 Cancer of the cervix uteri (ICD 180) Females, England and Wale

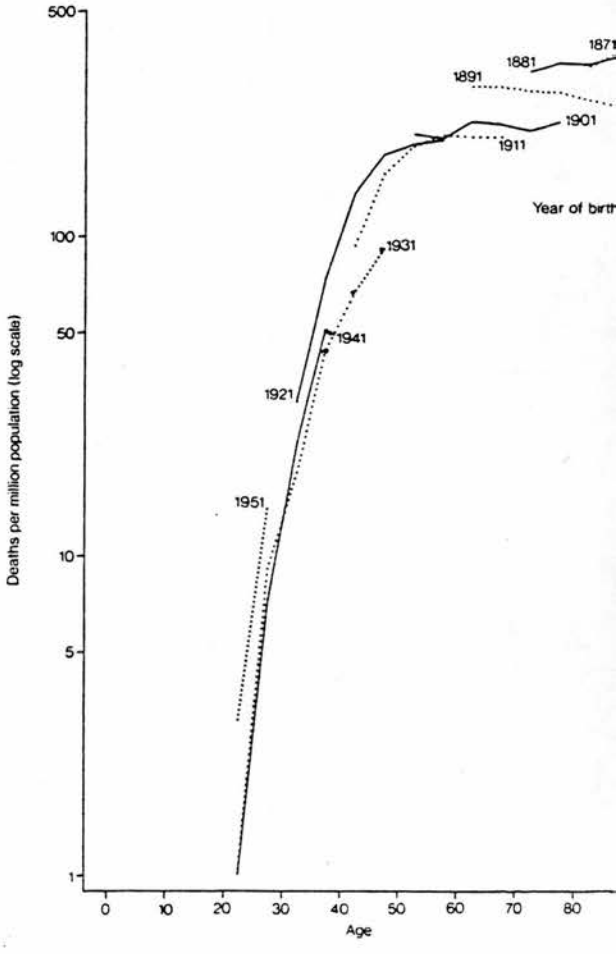
Table of deaths per million population with birth cohorts indicated on the diagonals

Year of death	Age-group 0-	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75-	80-	85 and over
1951-55	0	-	-	0	1	10	30	58	93	136	203	254	285	304	315	361	327	315
1956-60	0	-	0	0	1	9	37	74	119	154	181	197	246	284	313	336	366	361
1961-65	0	-	-	-	1	5	18	67	134	180	187	178	222	232	274	301	332	357
1966-70	0	-	-	0	2	7	15	44	104	176	204	201	193	217	247	271	290	351
1971-75	-	-	-	-	3	10	22	38	67	130	190	199	199	193	206	247	257	262
1976-78	-	-	-	0	2	14	30	51	59	91	175	198	217	198	209	220	249	247
Birth cohort (diagonal)					1956	1951	1946	1941	1936	1931	1926	1921	1916	1911	1906	1901	1896	

Graphs drawn from data in the table above to investigate and demonstrate cohort changes in mortality fro cancer of the cervix



Death rates presented so as to show changes within age-groups for varying years of birth



Death rates presented so as to show difference between birth cohorts at varying ages (alterna cohorts are omitted for clarity)

Source : Cancer Statistics : Studies on Medical and Population Subjects No. 43

1982, HMSO

Fig. 2.5

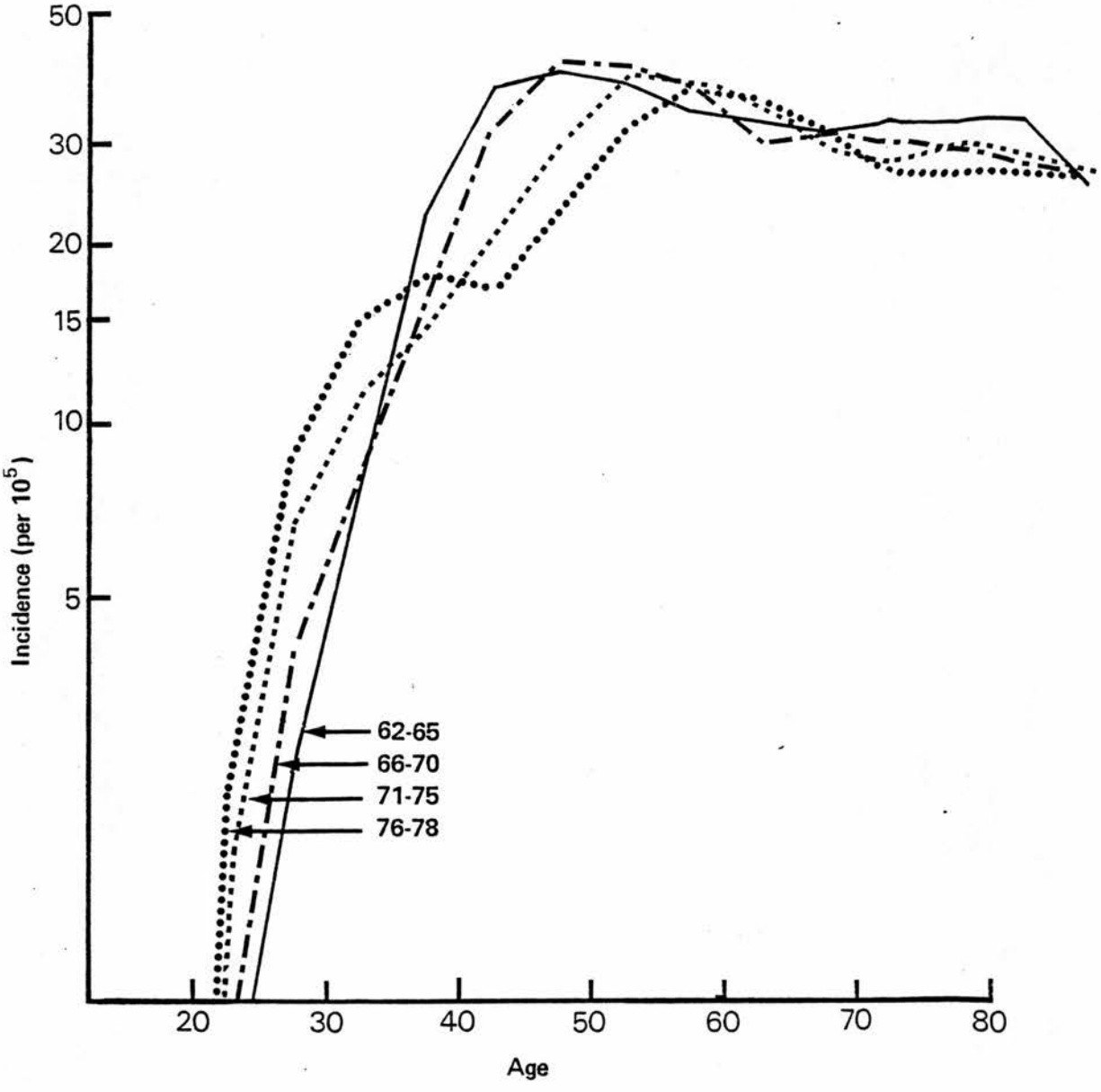

50
30
20
15
10
5
Incidence (per 10^5)
62-65
66-70
71-75
76-78
20
30
40
50
60
70
80
Age

Fig. 2.6

Year of incidence	AGE-GROUP													
	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75-	80-	85-
1961-1965	6	25	78	225	370	393	374	336	324	306	322	296	290	224
1966-1970	9	39	83	163	313	408	405	370	300	304	293	261	243	238
1971-1975	16	66	121	145	201	296	390	375	335	290	276	269	251	240
1976-1978	24	88	150	178	170	225	314	370	356	312	257	245	242	244
Birth cohort	1956	1951	1946	1941	1936	1931	1926	1921	1916	1911	1906	1901	1896	

1876
1881
1886
1891

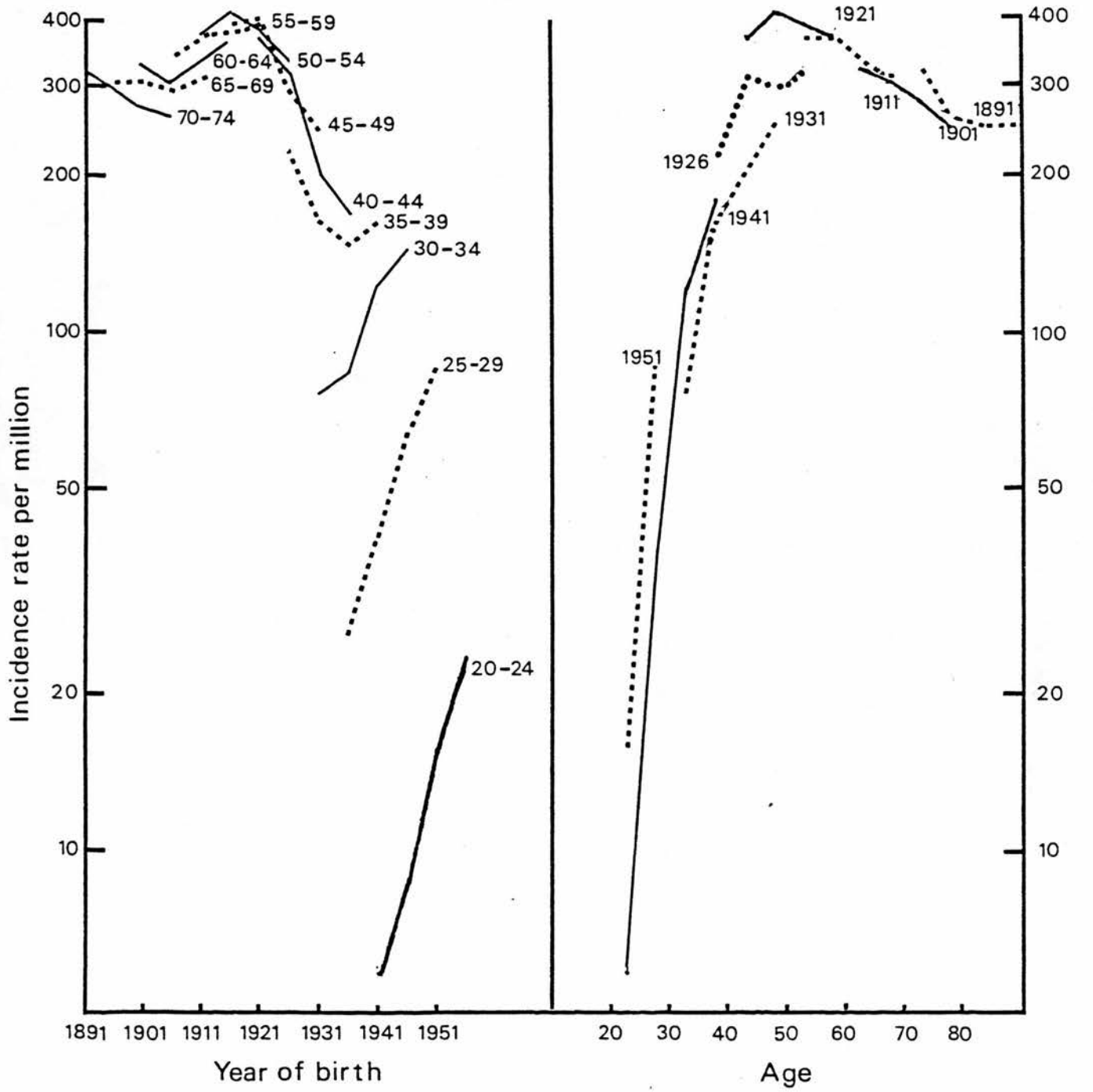


Fig 2.7 Age-specific Prevalence of Dysplasia

(Leeds/Wakefield data shows 95% confidence limits)

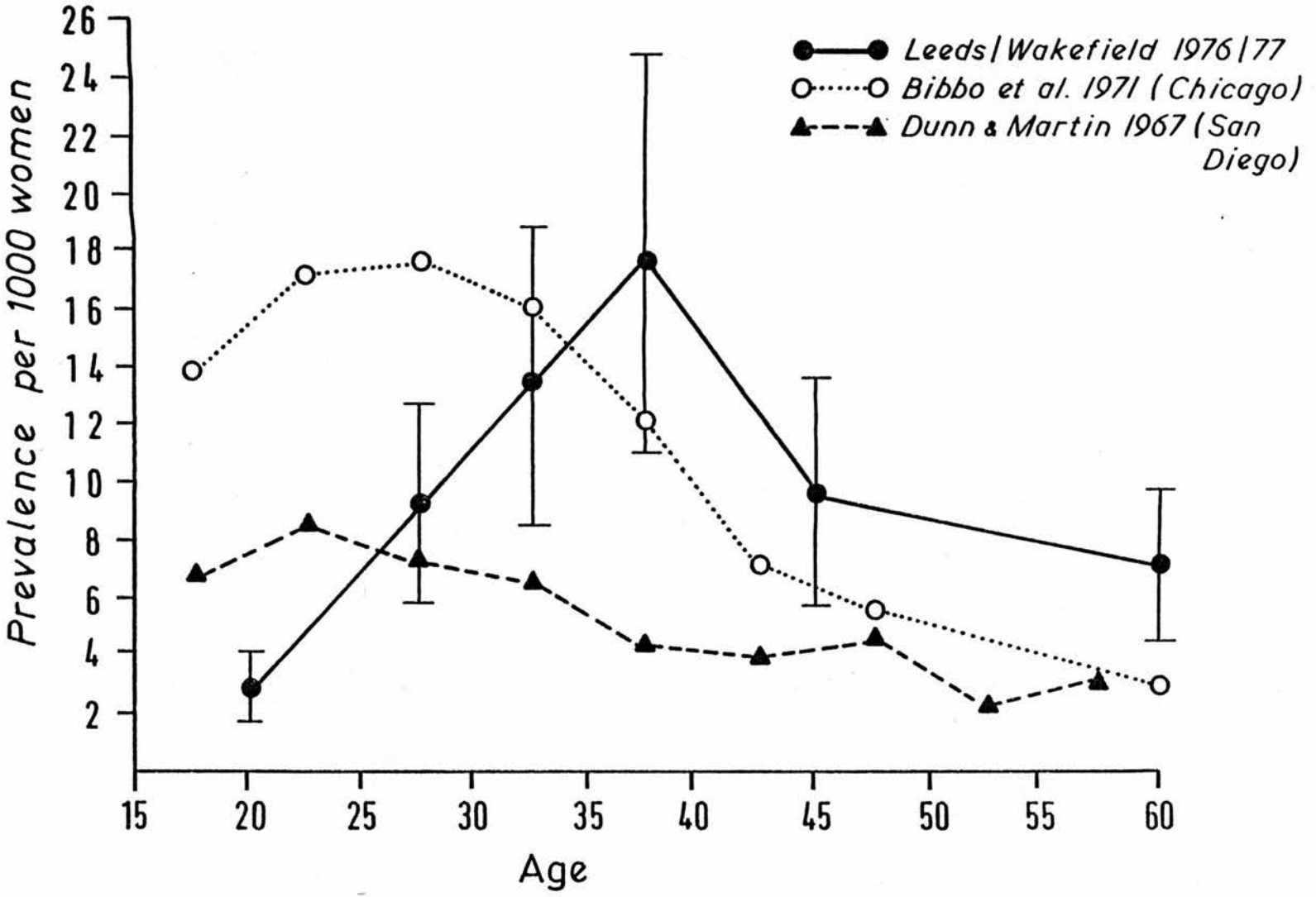


Fig 2.8 Age-specific Prevalence of Carcinoma in-situ

(Leeds/Wakefield data shows 95% confidence limits)

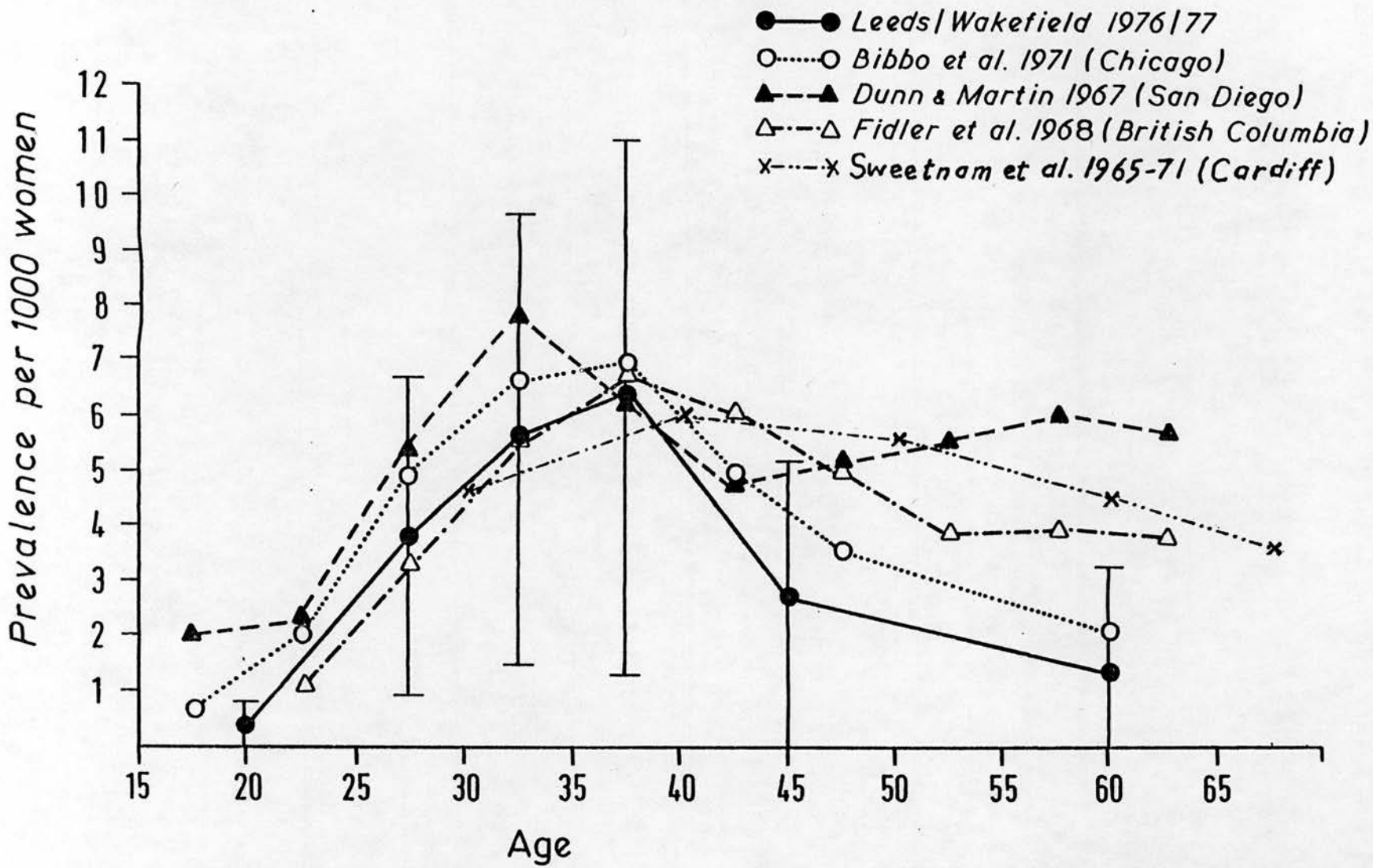
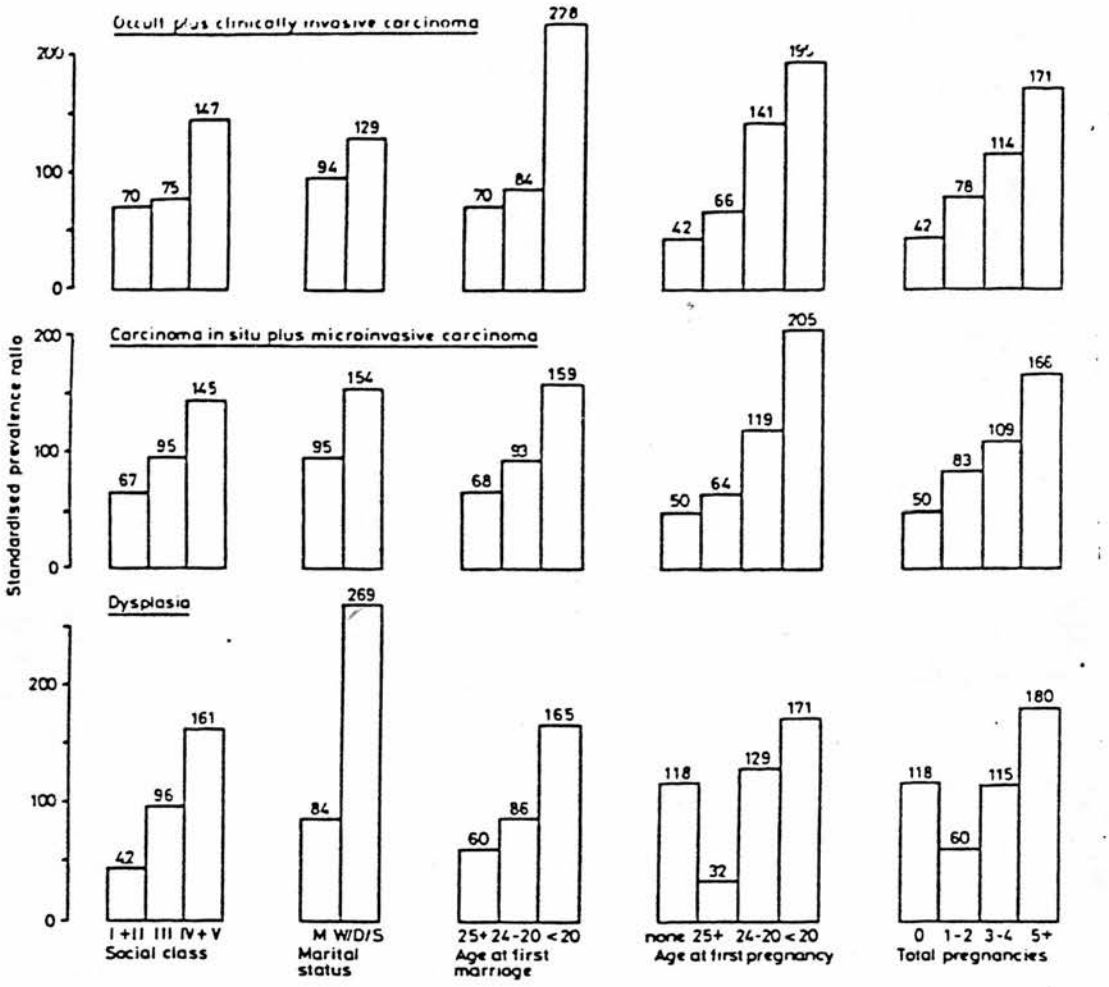


Fig 2.9



Source : Sweetnam et al (1981)

Fig 2.10 Age-specific Incidence of Dysplasia (Leeds/Wakefield data shows 95% confidence limits)

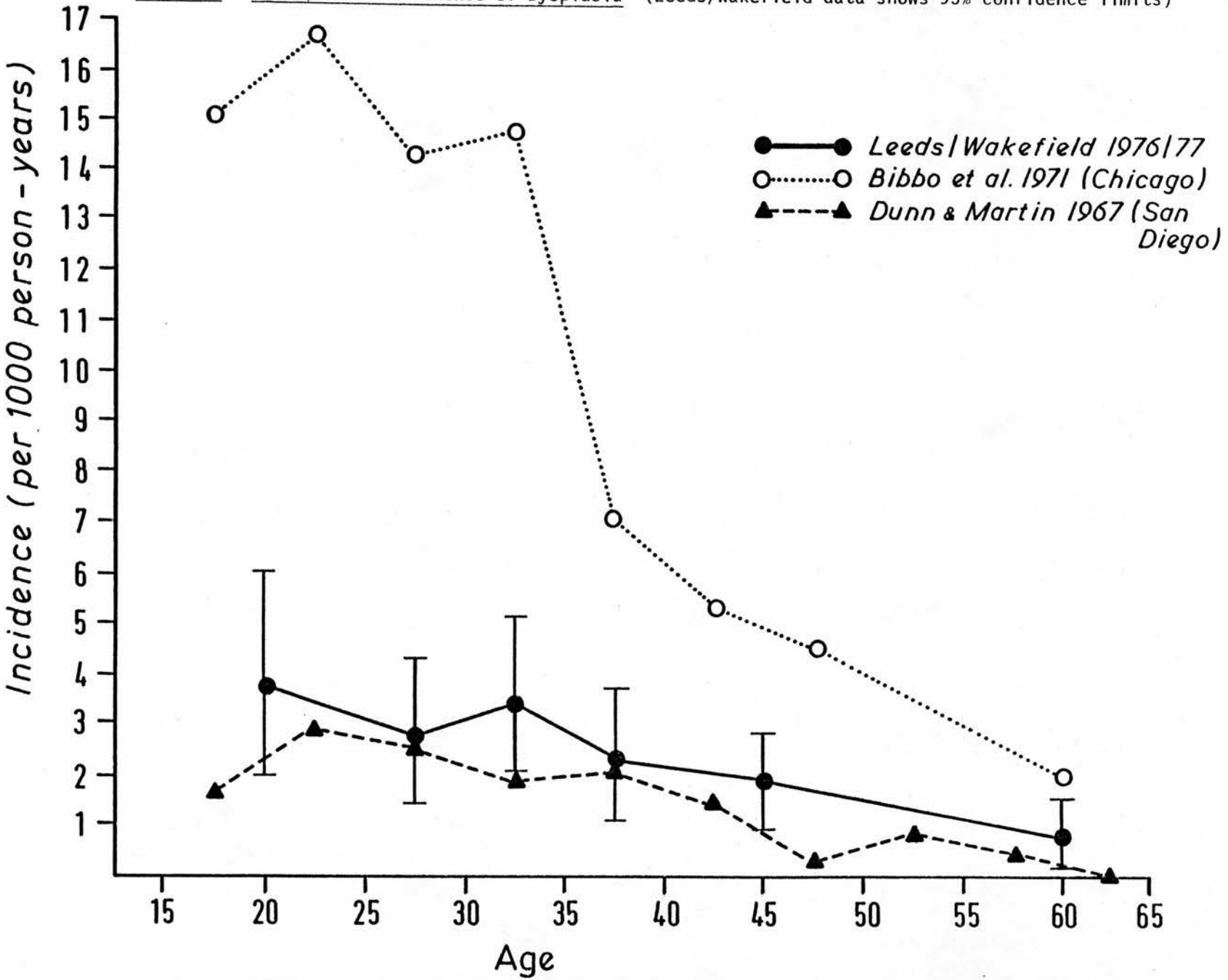


Fig 2.11 Age-specific Incidence of Carcinoma in-situ

(Leeds/Wakefield data shows 95% confidence limits)

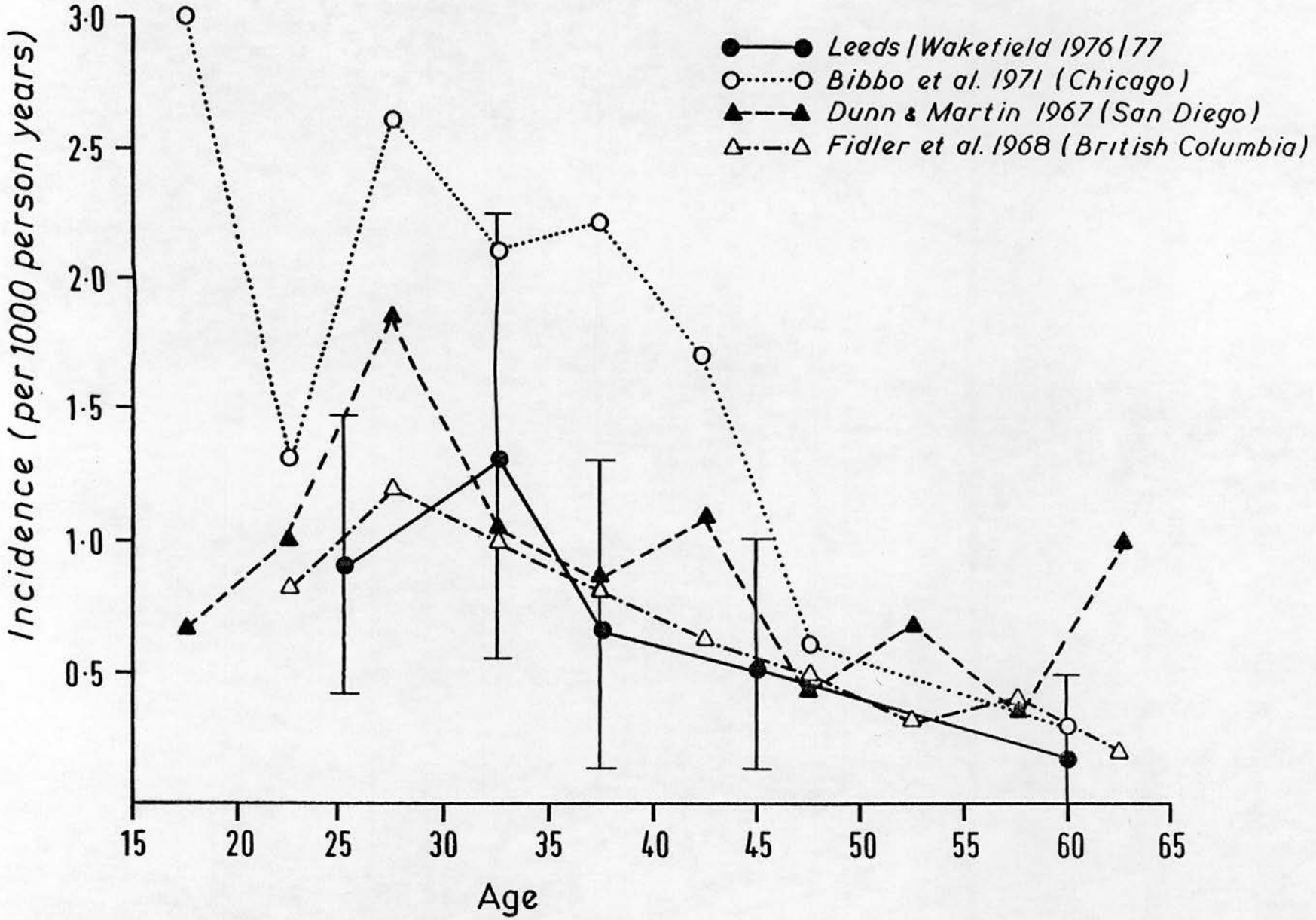


Fig. 2.12

RELATIONSHIP BETWEEN INCIDENT IN SITU CANCER & OUTCOME

Data : Fidler & Boyes, 1968 (British Columbia)

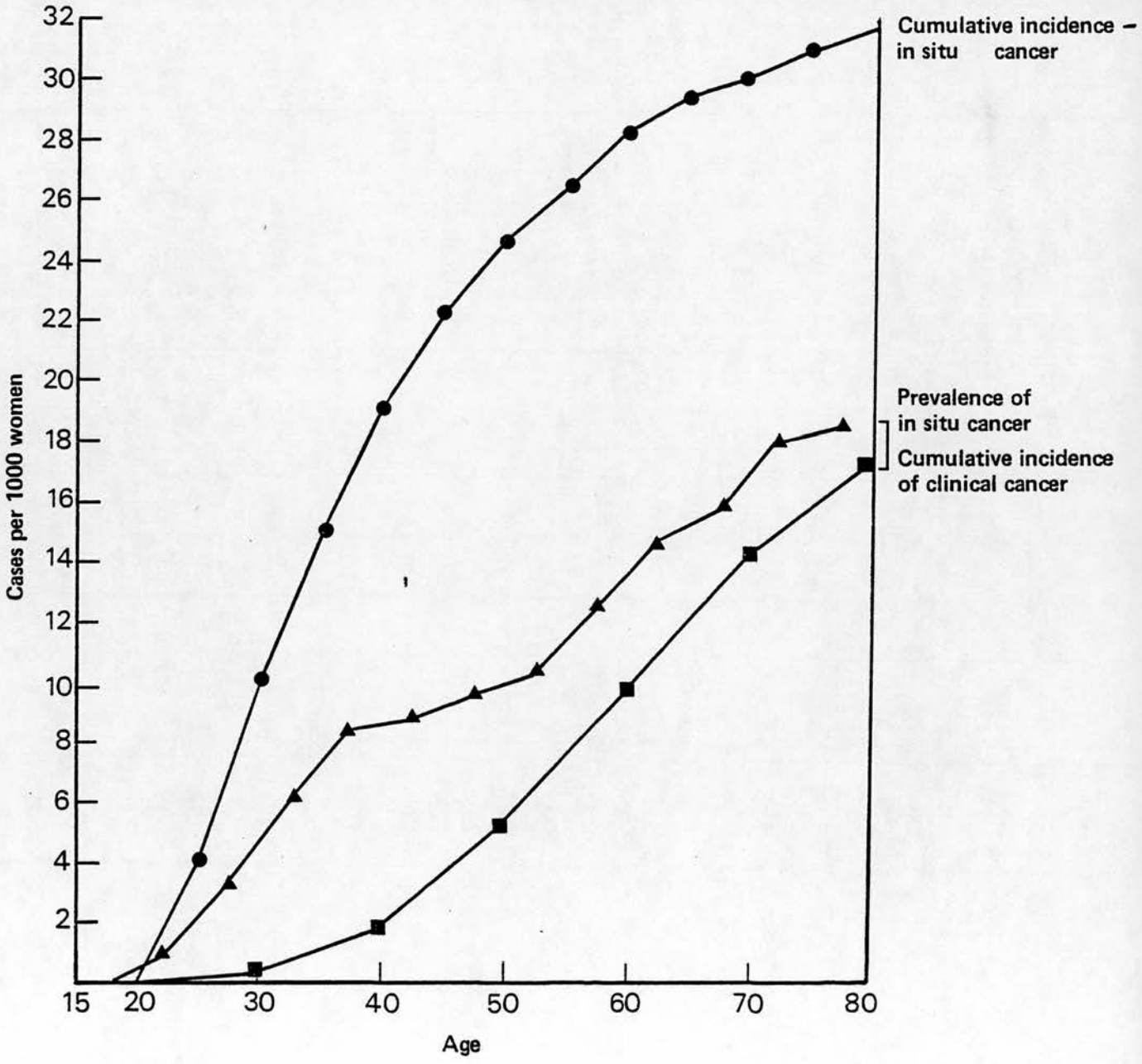
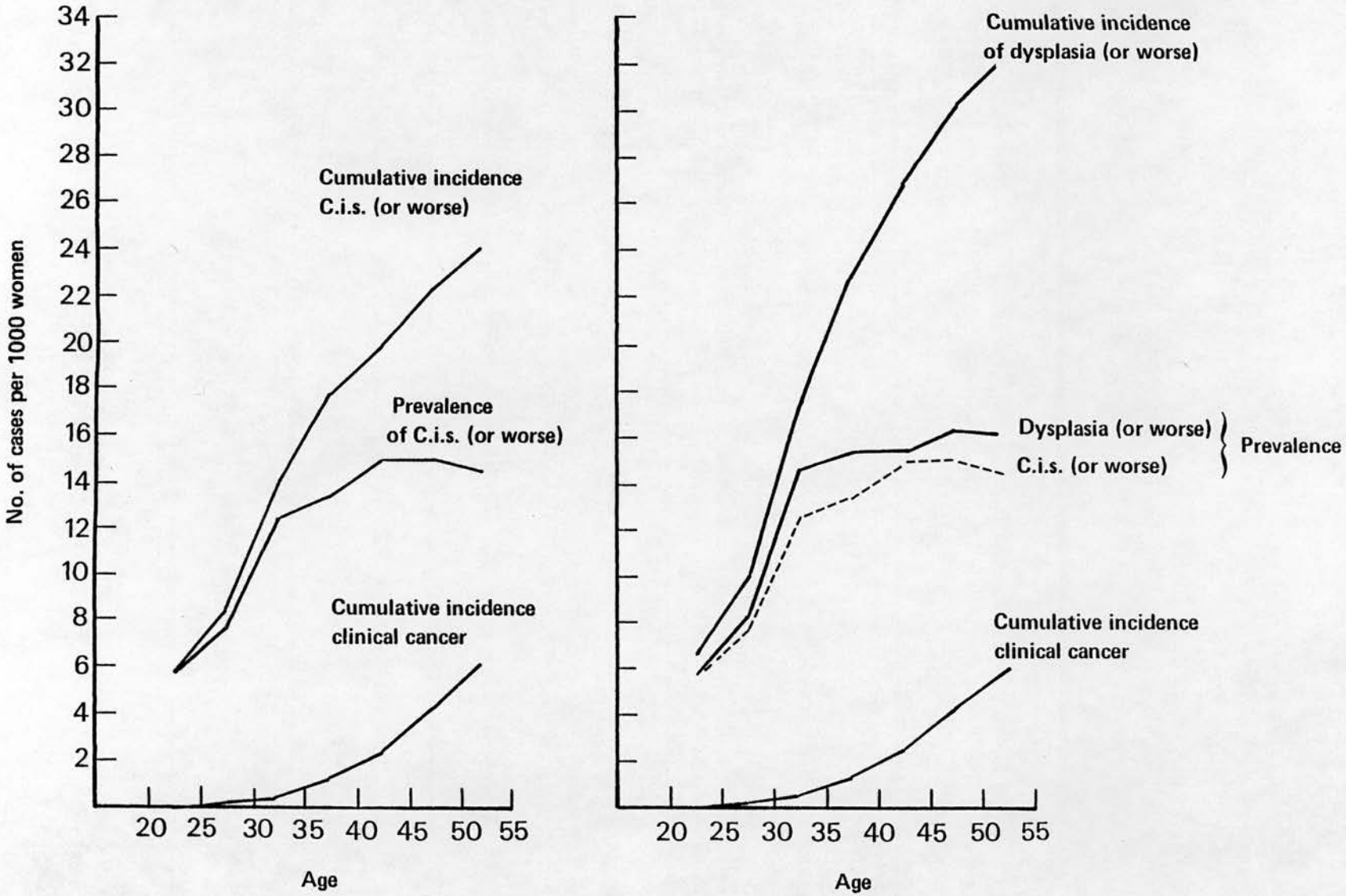
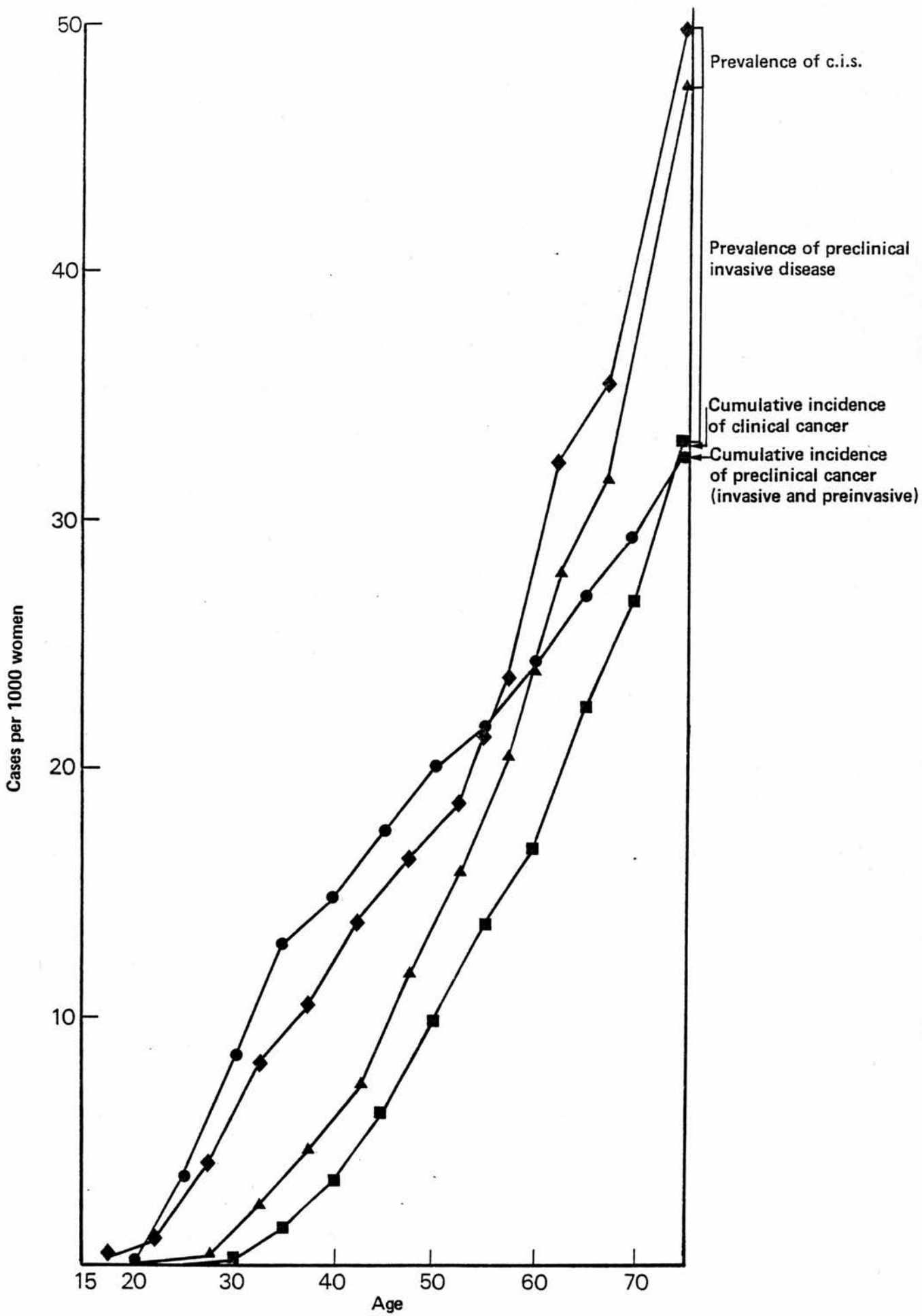


Fig 2.13

Data from British Columbia Cohort Study (Boyes et al 1982)



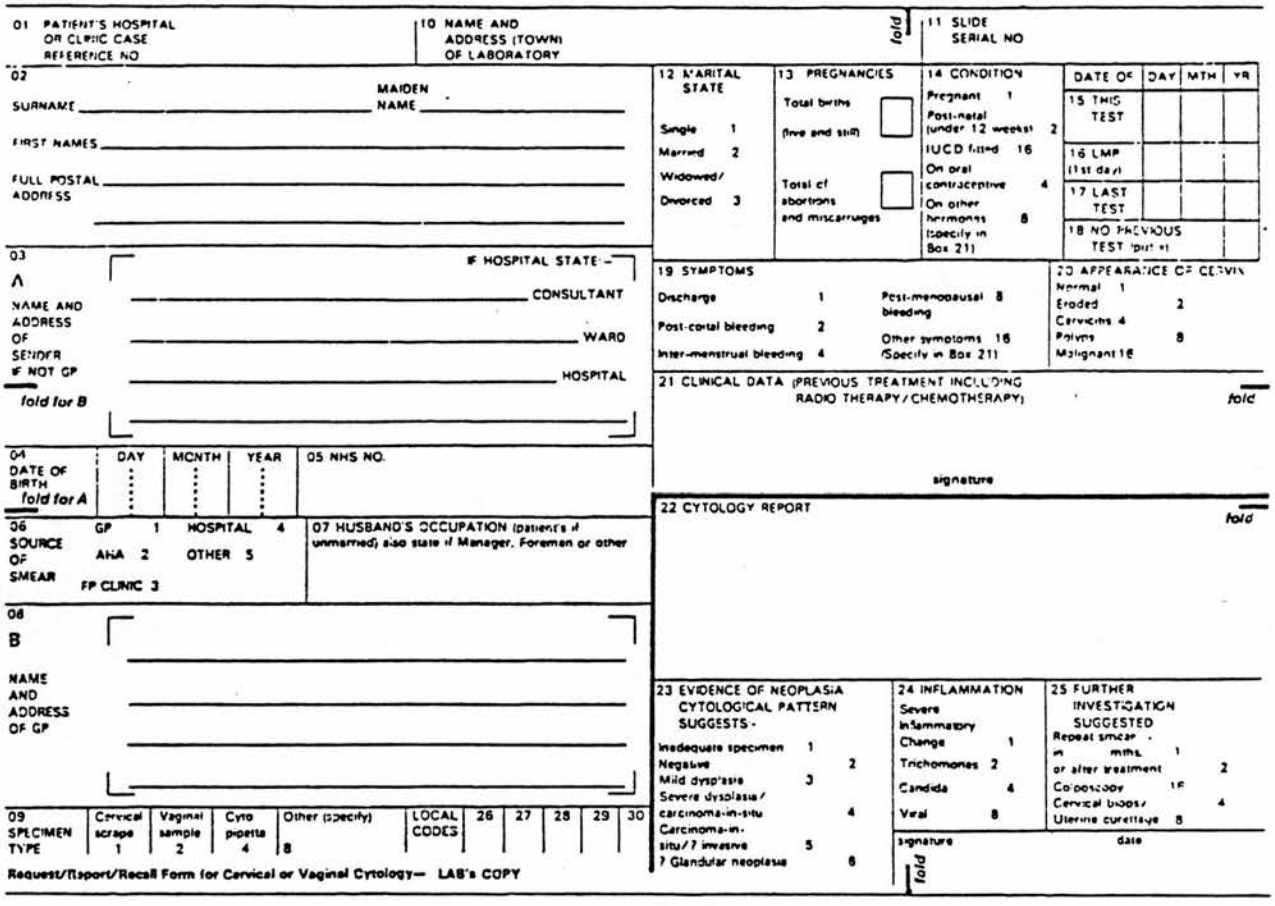


ig. 2.14

RELATIONSHIP BETWEEN INCIDENCE OF PRECLINICAL DISEASE AND OUTCOME

Data of Kashgarian & Dunn (1970)

Fig 2.15



01 PATIENT'S HOSPITAL OR CLINIC CASE REFERENCE NO

10 NAME AND ADDRESS (TOWN) OF LABORATORY

fold

11 SLIDE SERIAL NO

02

SURNAME _____ MAIDEN NAME _____

FIRST NAMES _____

FULL POSTAL ADDRESS _____

12 MARITAL STATE

Single 1
Married 2
Widowed/ Divorced 3

13 PREGNANCIES

Total births (live and still) ☐

Total of abortions and miscarriages ☐

14 CONDITION

Pregnant 1
Post-natal (under 12 weeks) 2
IUCD fitted 16
On oral contraceptive 4
On other hormones 8
(specify in Box 21)

DATE OF	DAY	MTH	YR
15 THIS TEST			
16 LMP (1st day)			
17 LAST TEST			
18 NO PREVIOUS TEST (put x)			

03

A

IF HOSPITAL STATE:-

NAME AND ADDRESS OF SENDER IF NOT GP

CONSULTANT _____

WARD _____

HOSPITAL _____

fold for B

19 SYMPTOMS

Discharge 1
Post-coital bleeding 2
Inter-menstrual bleeding 4
Post-menopausal bleeding 8
Other symptoms 16
(Specify in Box 21)

20 APPEARANCE OF CERVIX

Normal 1
Eroded 2
Cervicitis 4
Polyps 8
Malignant 16

21 CLINICAL DATA (PREVIOUS TREATMENT INCLUDING RADIO THERAPY/CHEMOTHERAPY)

fold

04 DATE OF BIRTH fold for A — DAY | MONTH | YEAR

05 NHS NO.

signature

22 CYTOLOGY REPORT

fold

06 SOURCE OF SMEAR

GP 1
AHA 2
FP CLINIC 3
HOSPITAL 4
OTHER 5

07 HUSBAND'S OCCUPATION (patient's if unmarried) also state if Manager, Foreman or other

08

B

NAME AND ADDRESS OF GP

23 EVIDENCE OF NEOPLASIA CYTOLOGICAL PATTERN SUGGESTS:-

Inadequate specimen 1
Negative 2
Mild dyskaryosis 3
Severe dyskaryosis / carcinoma-in-situ 4
Carcinoma-in-situ / ? invasive 5
? Glandular neoplasia 6

24 INFLAMMATION

Severe inflammatory Change 1
Trichomonas 2
Candida 4
Viral 8

25 FURTHER INVESTIGATION SUGGESTED

Repeat smear in mths 1
or after treatment 2
Colposcopy 1F
Cervical biopsy 4
Uterine curettage 8

signature

date

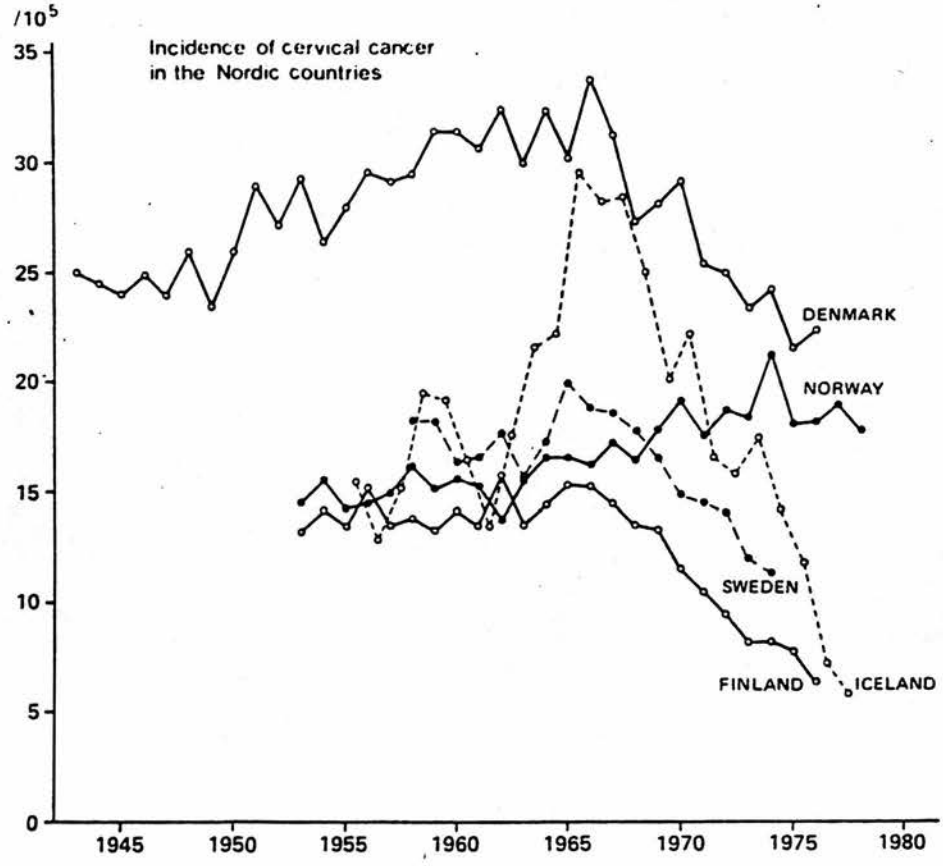
fold

09 SPECIMEN TYPE	Cervical scrape 1	Vaginal sample 2	Cyto pipette 4	Other (specify) 8	LOCAL CODES	26	27	28	29	30

Request/Report/Recall Form for Cervical or Vaginal Cytology— LAB's COPY

National recall scheme – form H.M.R. 101/5 (1977).

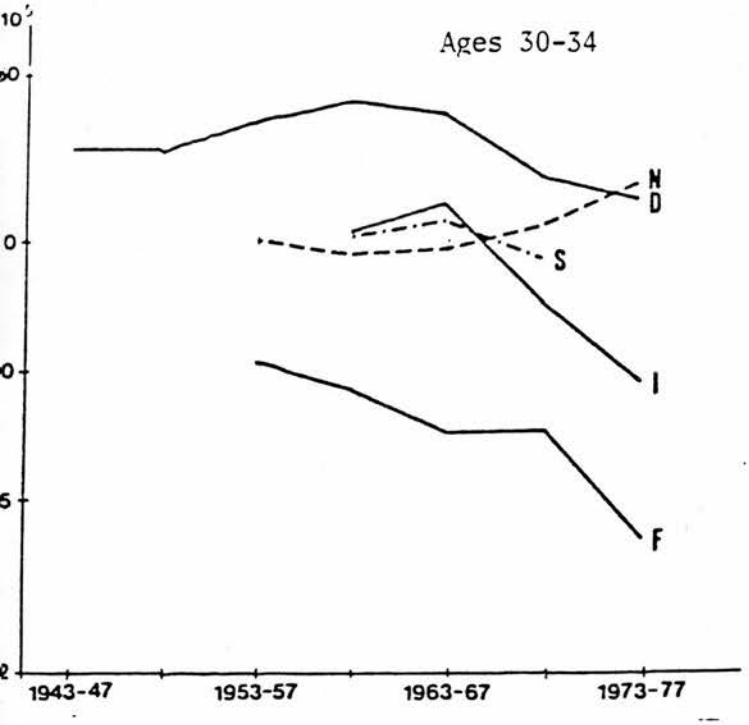
Fig 2.16

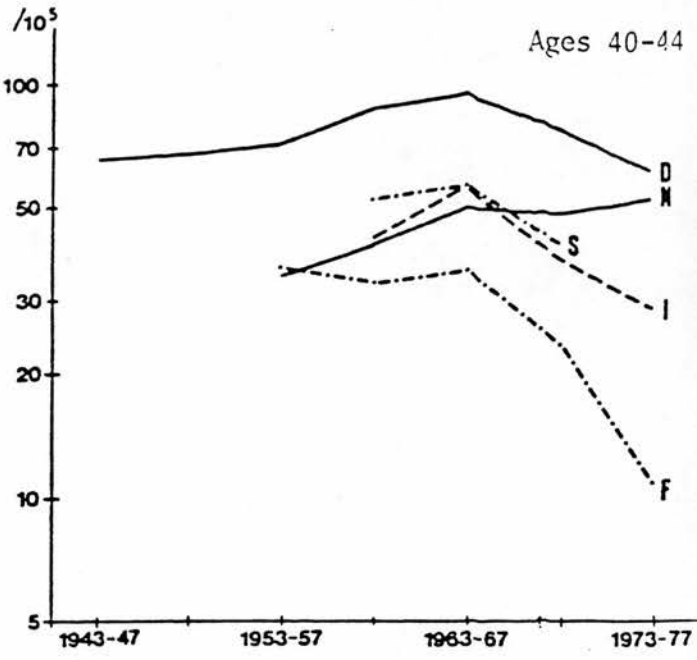


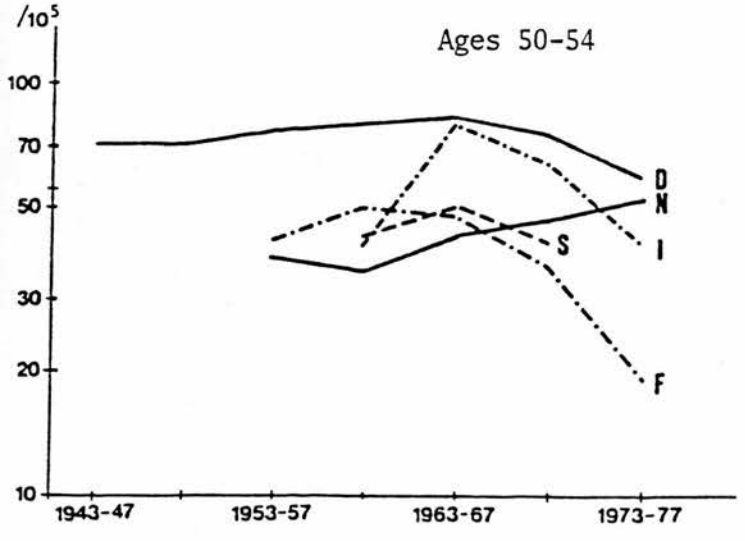
Annual incidences of cervical cancer in the Nordic countries in 1943–1978.

Fig 2.17

TRENDS IN CANCER INCIDENCE IN THE NORDIC COUNTRIES







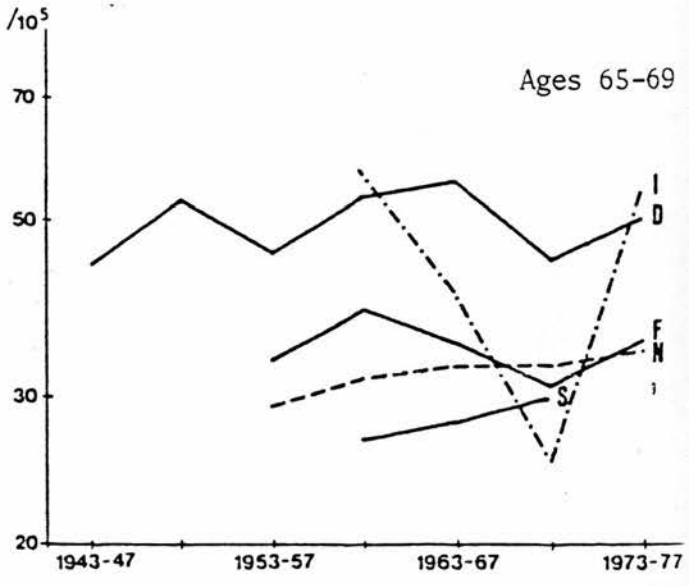


Fig 2.18 Incidence rates for cervix cancer, by birth cohort (England & Wales) per 10^5 uteri at risk. (Parkin et al, 1984)

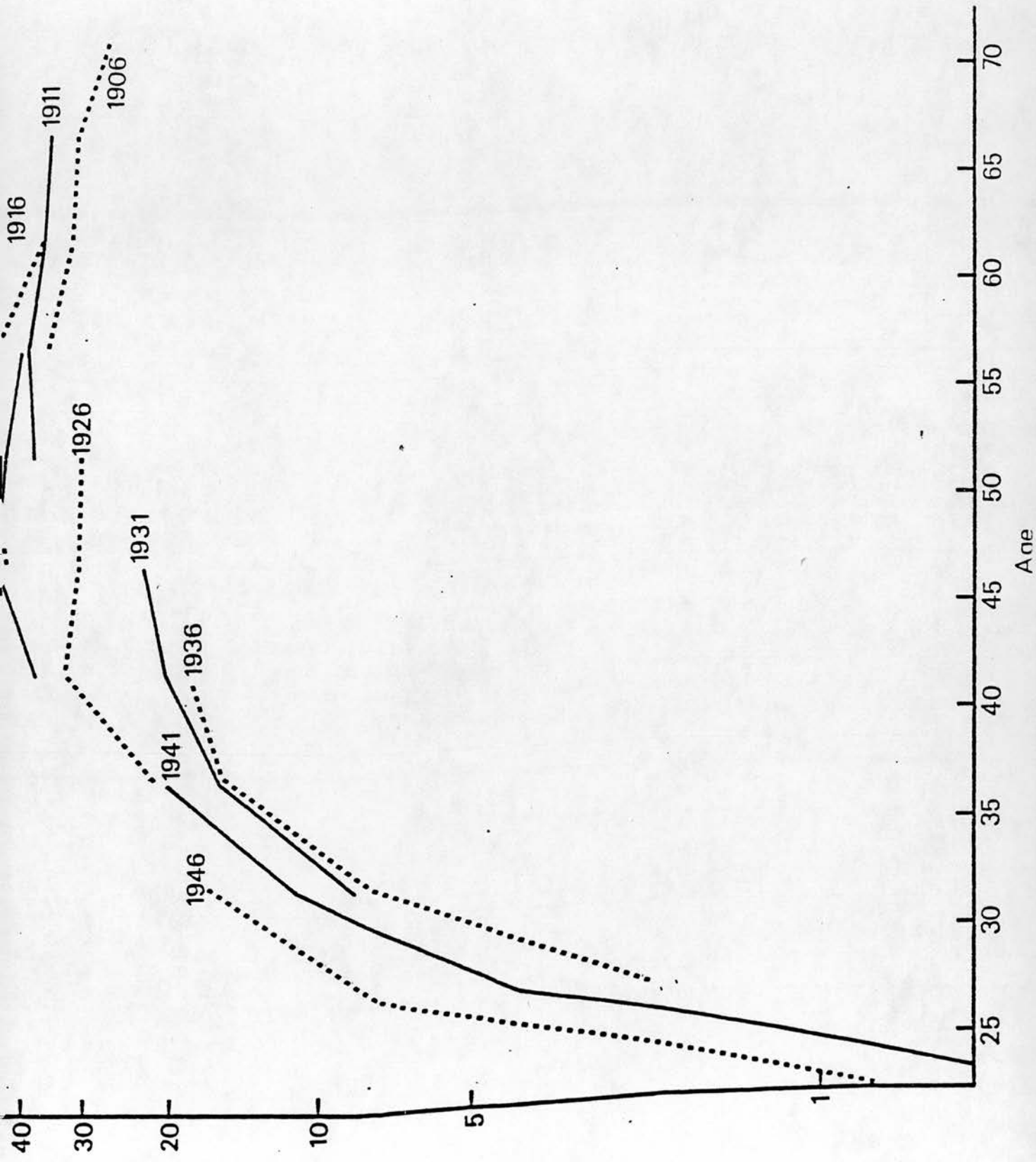


Fig 2.19 Incidence predicted in absence of screening (per 10^5 uteri at risk)
(from Parkin et al, 1984)

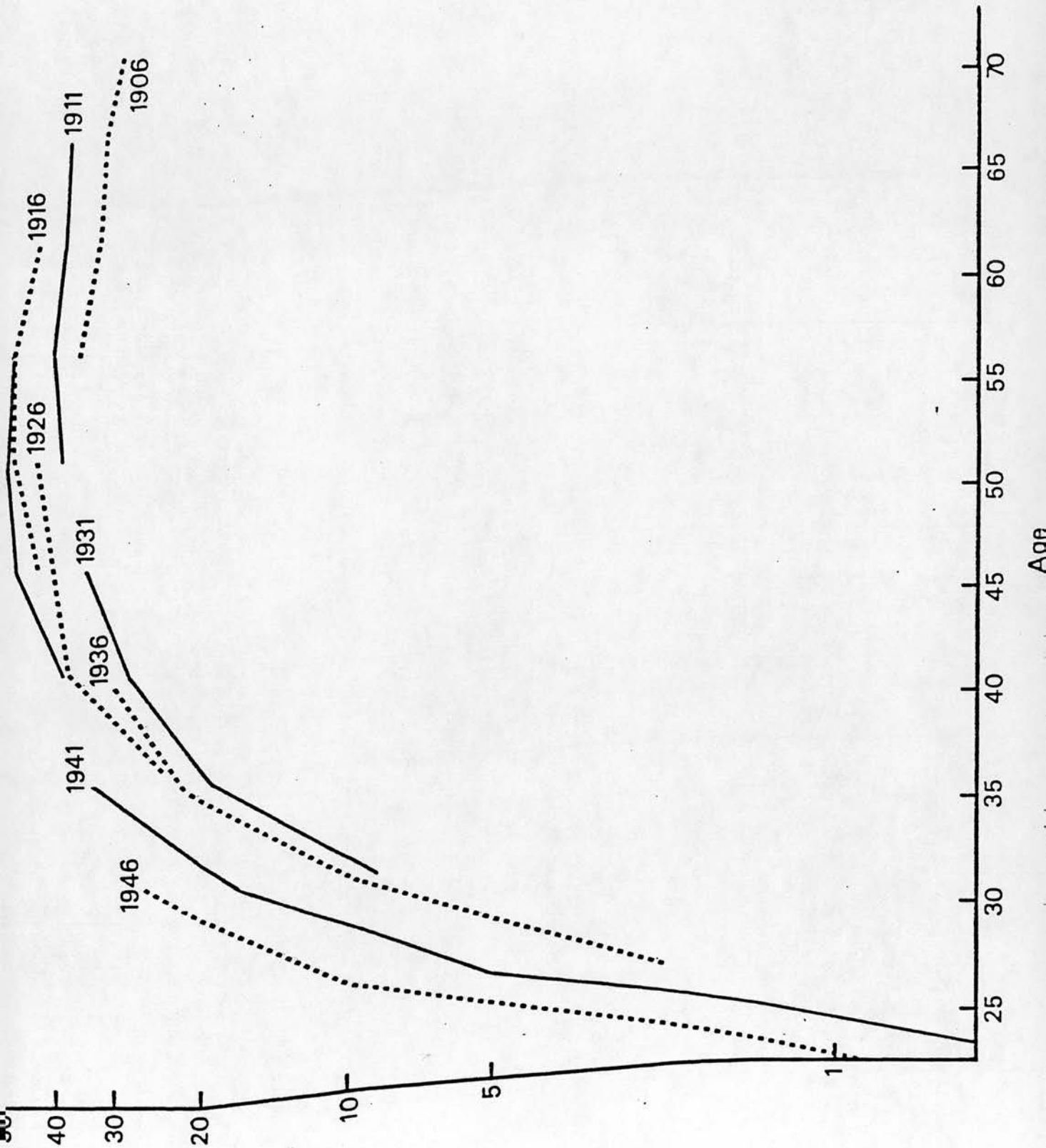
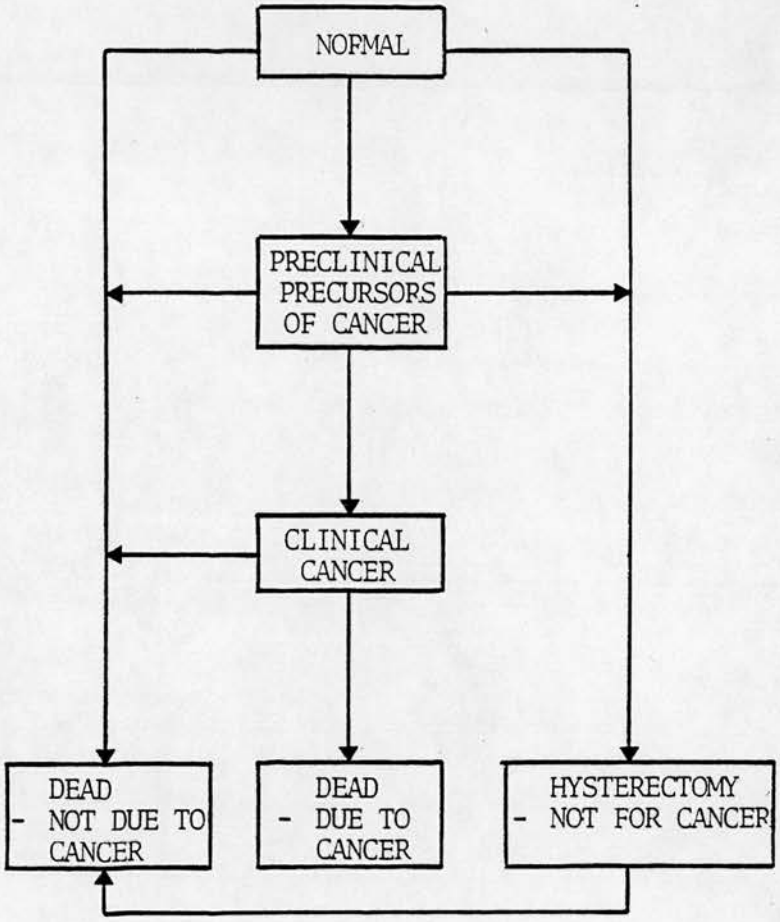


Fig 4.1

SIMPLE MODEL OF DISEASE NATURAL HISTORY



NATURAL HISTORY : EXAMPLE OF STATES USED IN SIMULATION

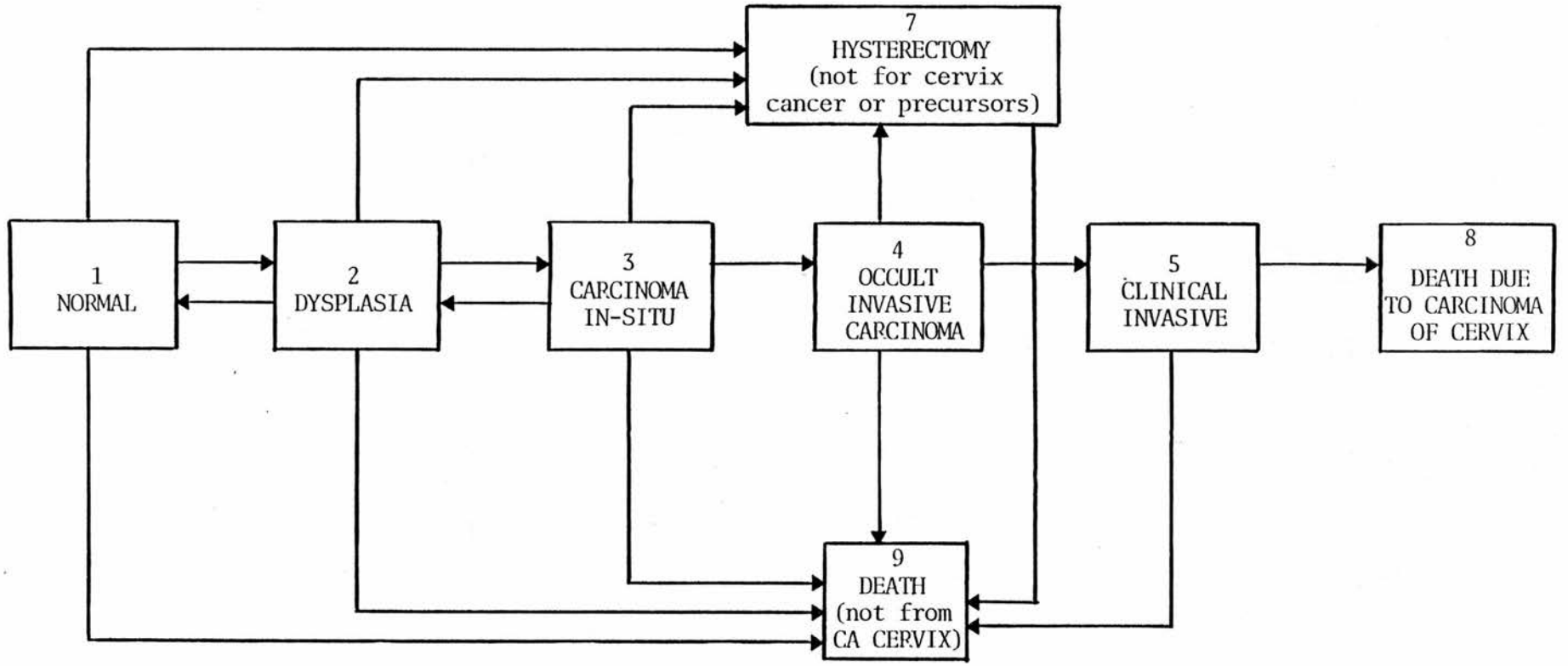


Fig. 4.5

RELATIVE SURVIVAL, CARCINOMA OF CERVIX : 1971-1973 ENGLAND & WALES

Source : Cancer Statistics 1971-1973 : Survival (OPCS, series MB1 No 3)

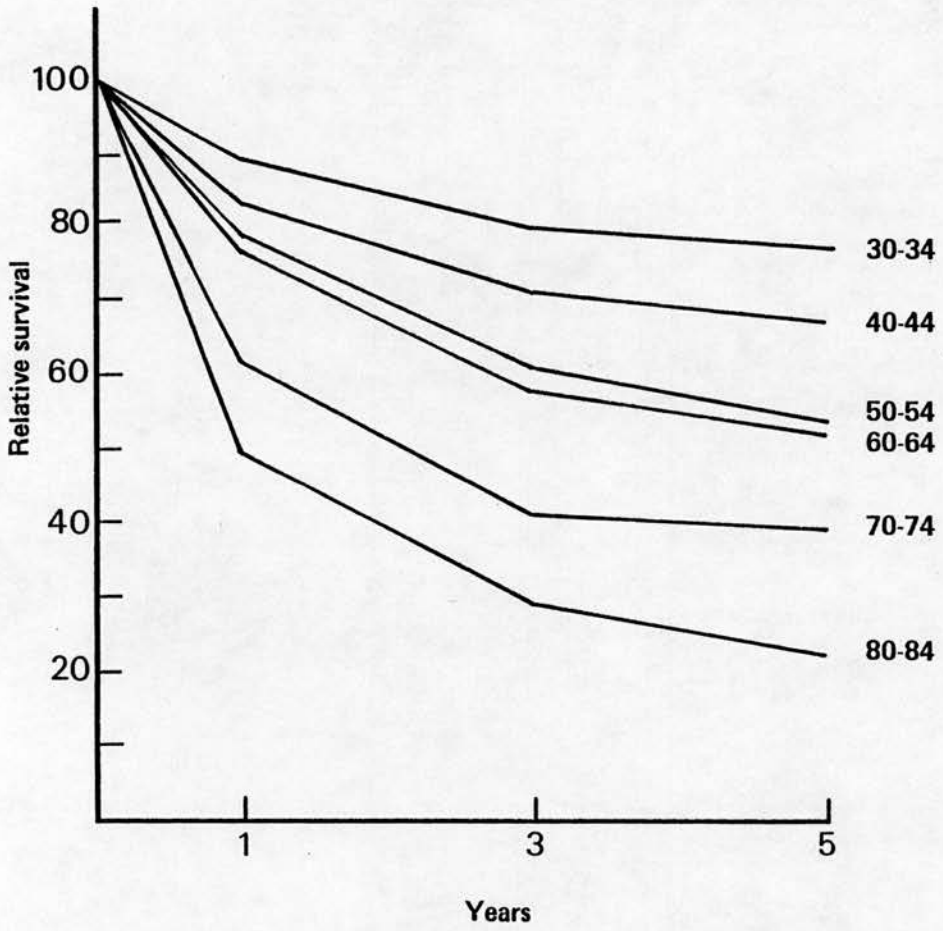


Fig 4.4 Sojourn times of dysplasia

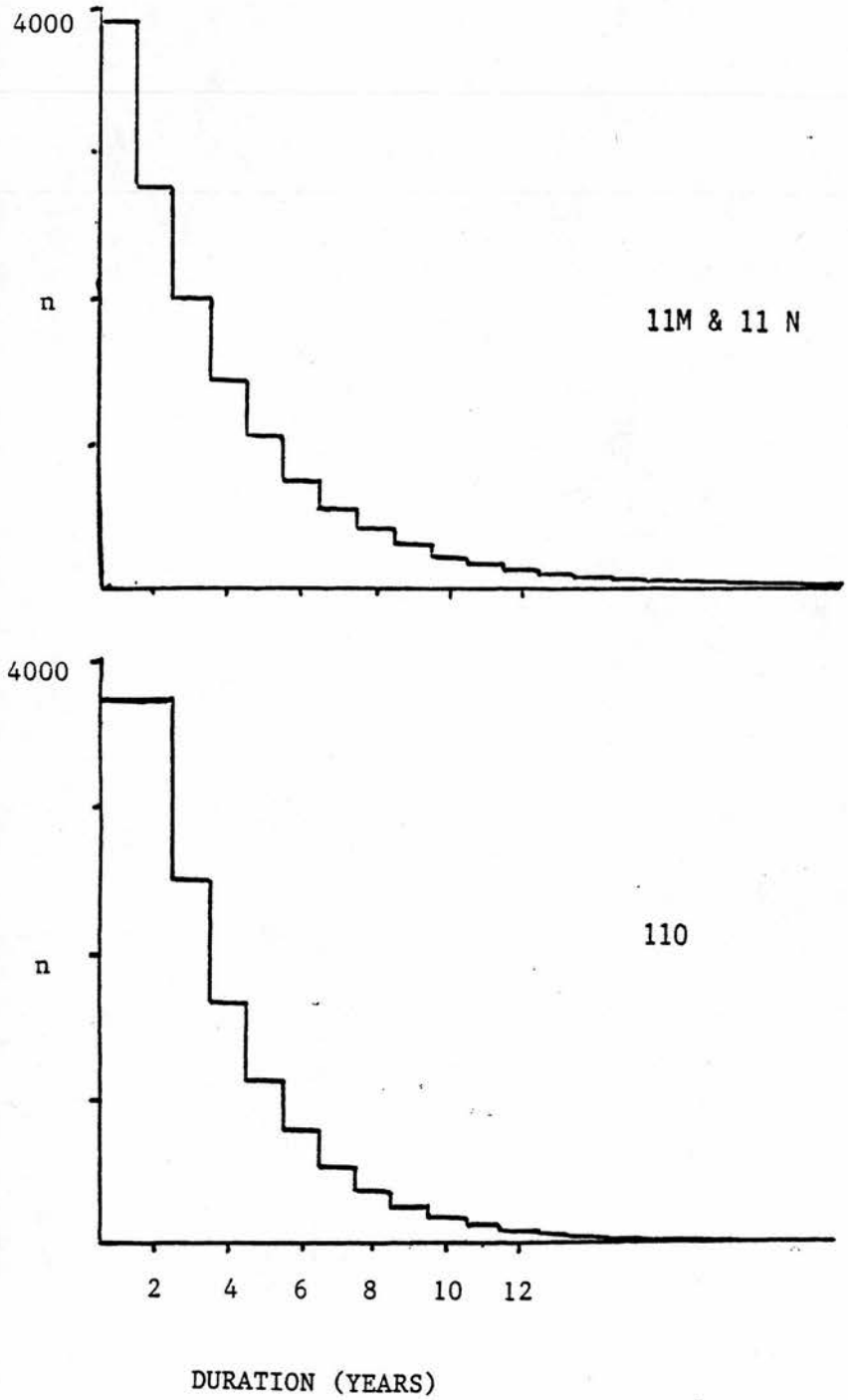


Fig 4.5 Sojourn times of Carcinoma in Situ

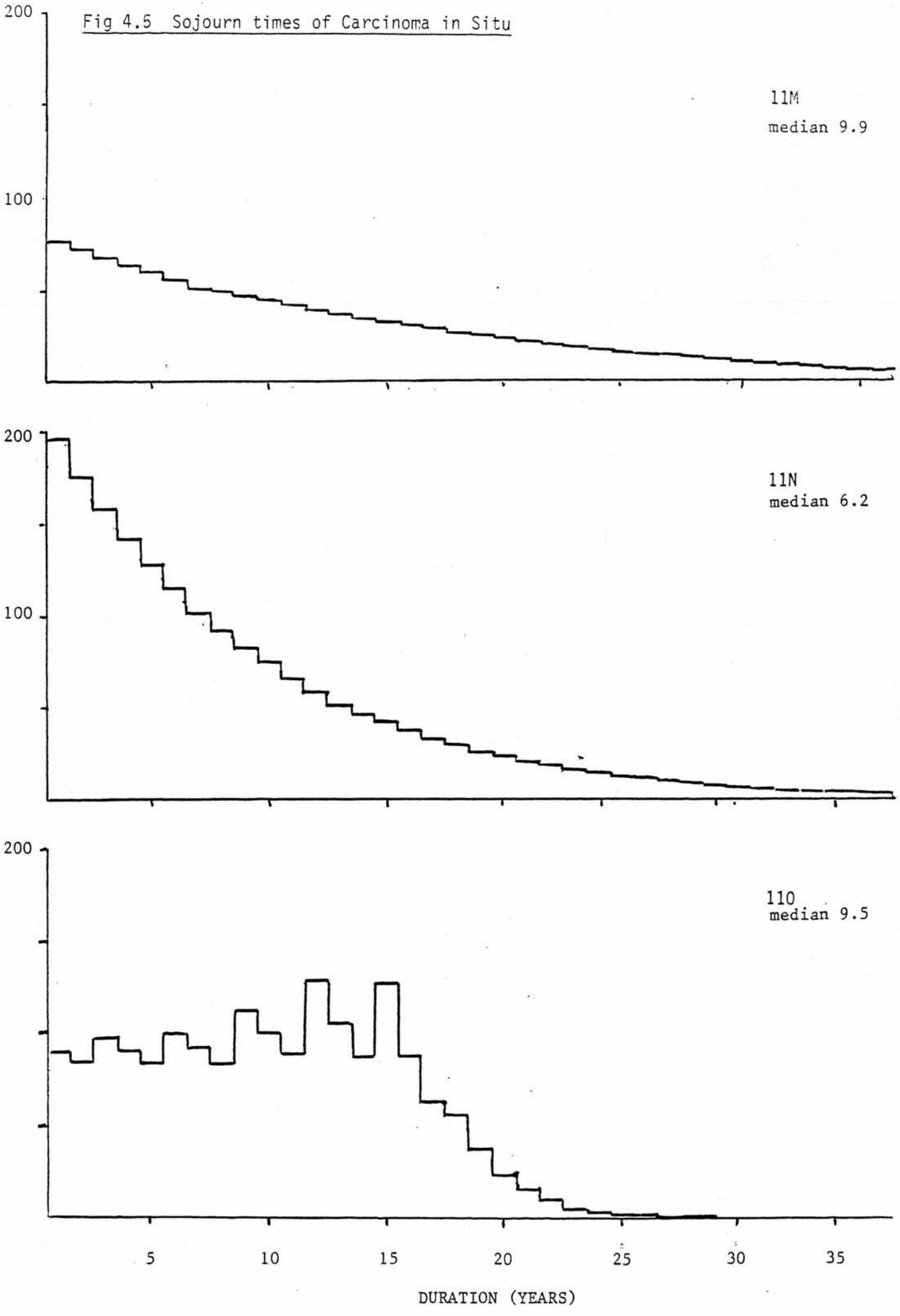
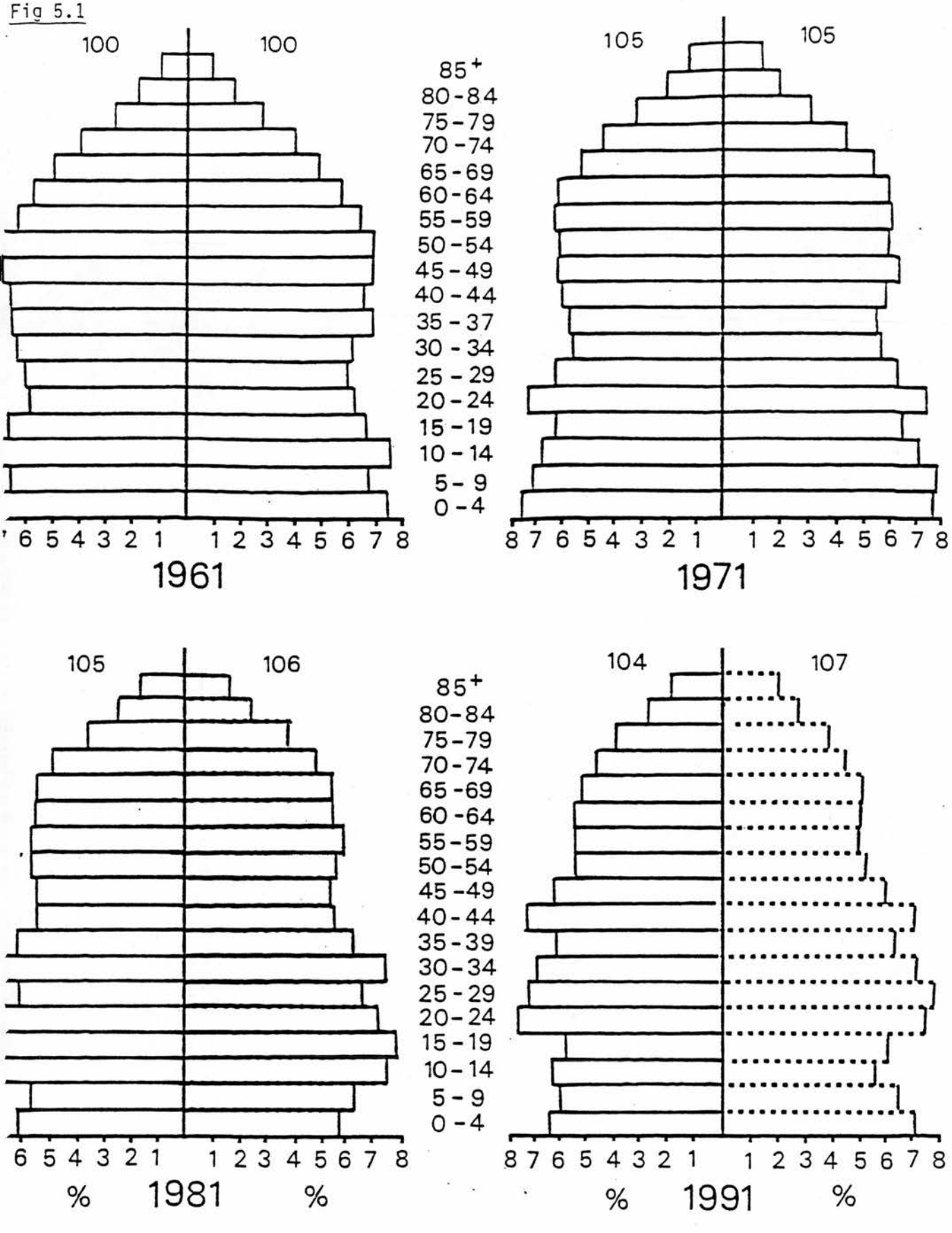


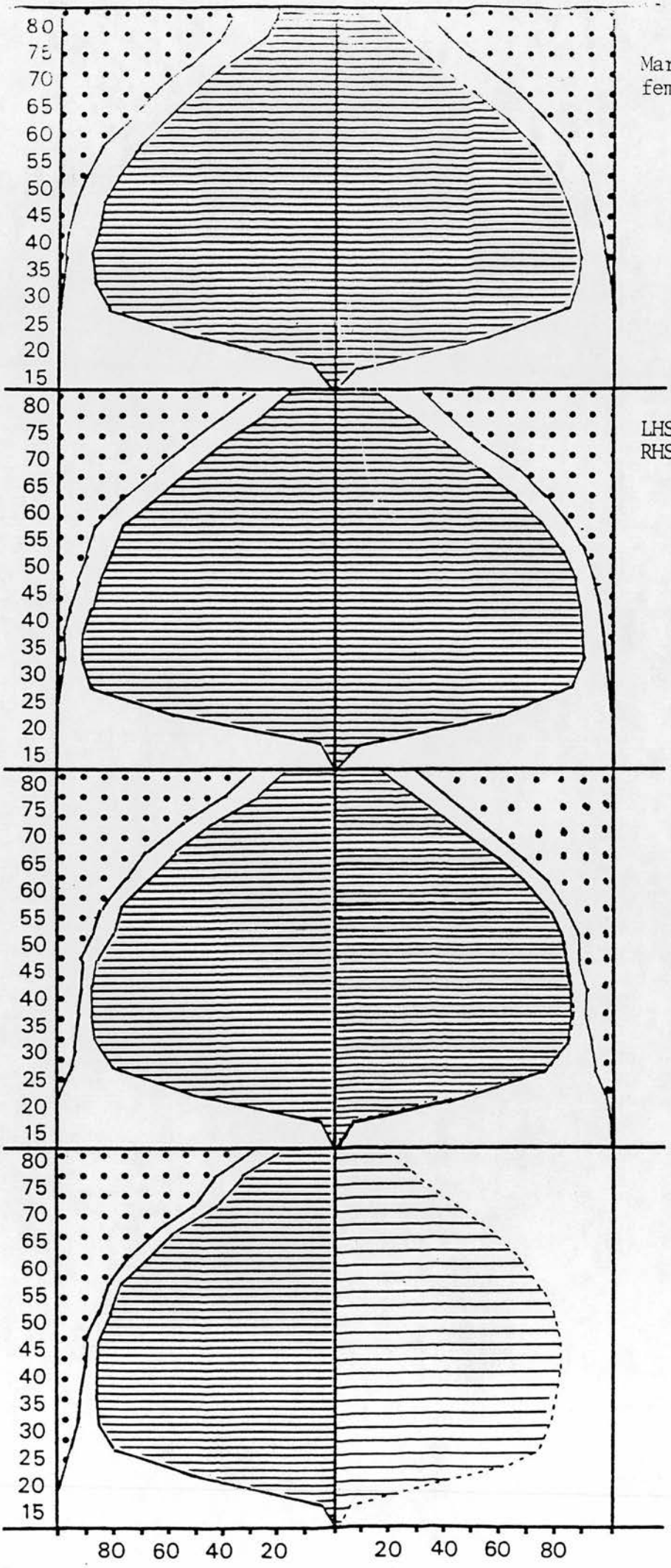
Fig 5.1



Female population (England and Wales) by age

L : model predictions
R : census data (1961, 1971, 1981)
projections (1991)

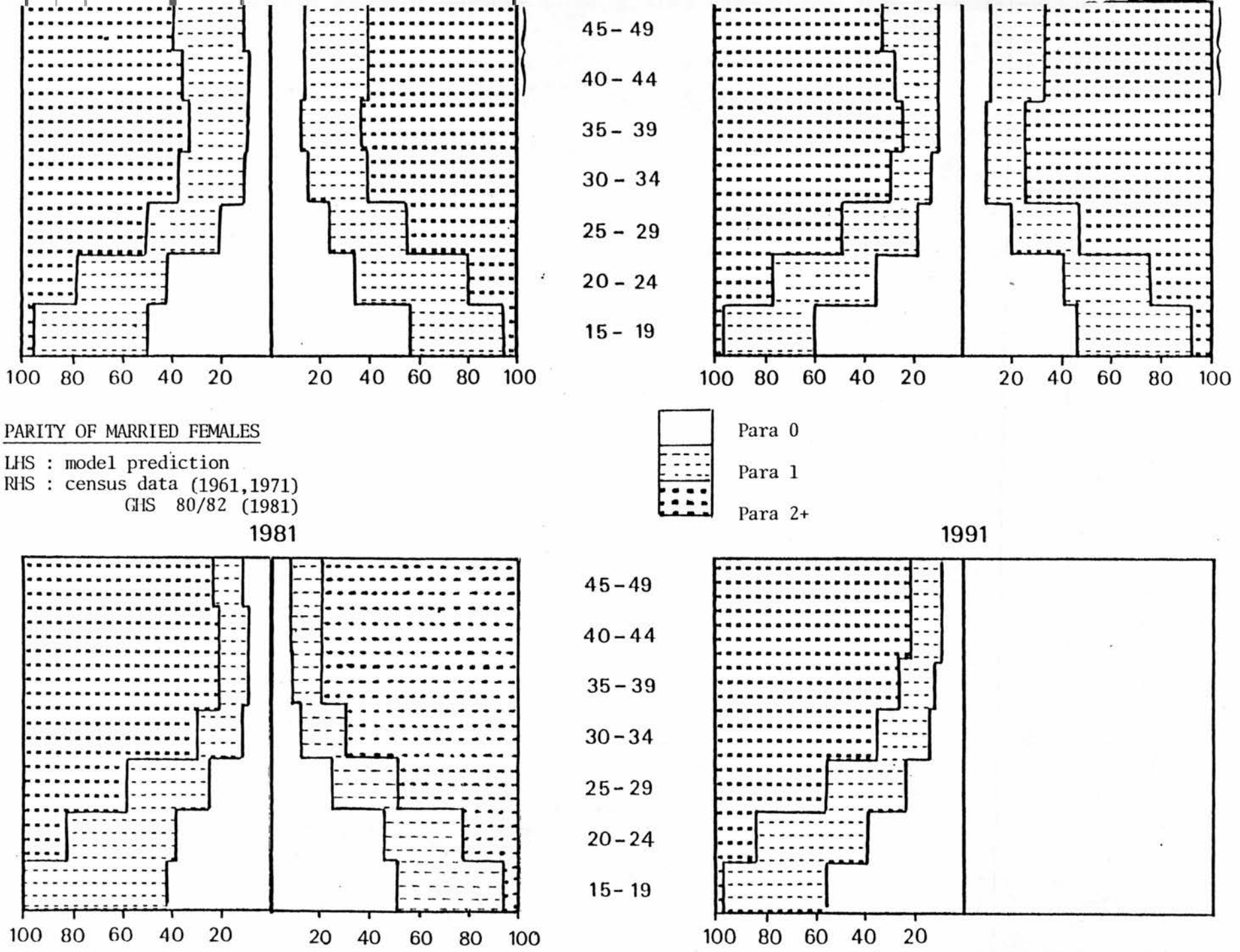
Fig 5.2



Marital composition of female population (by age)

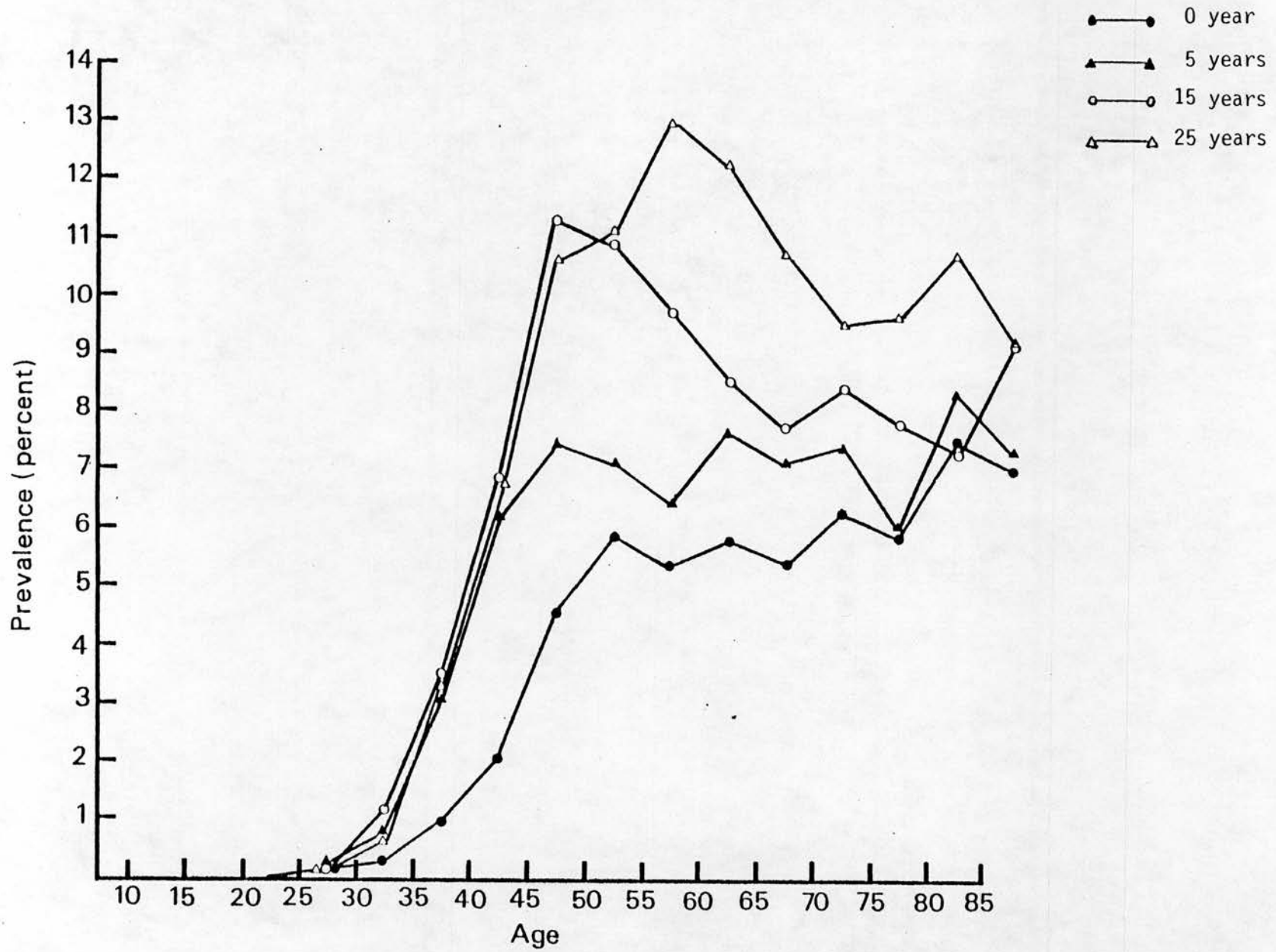
Single
Married
Formerly married

LHS : model predictions
RHS : census data (1961, 71, 81
projections (1991)

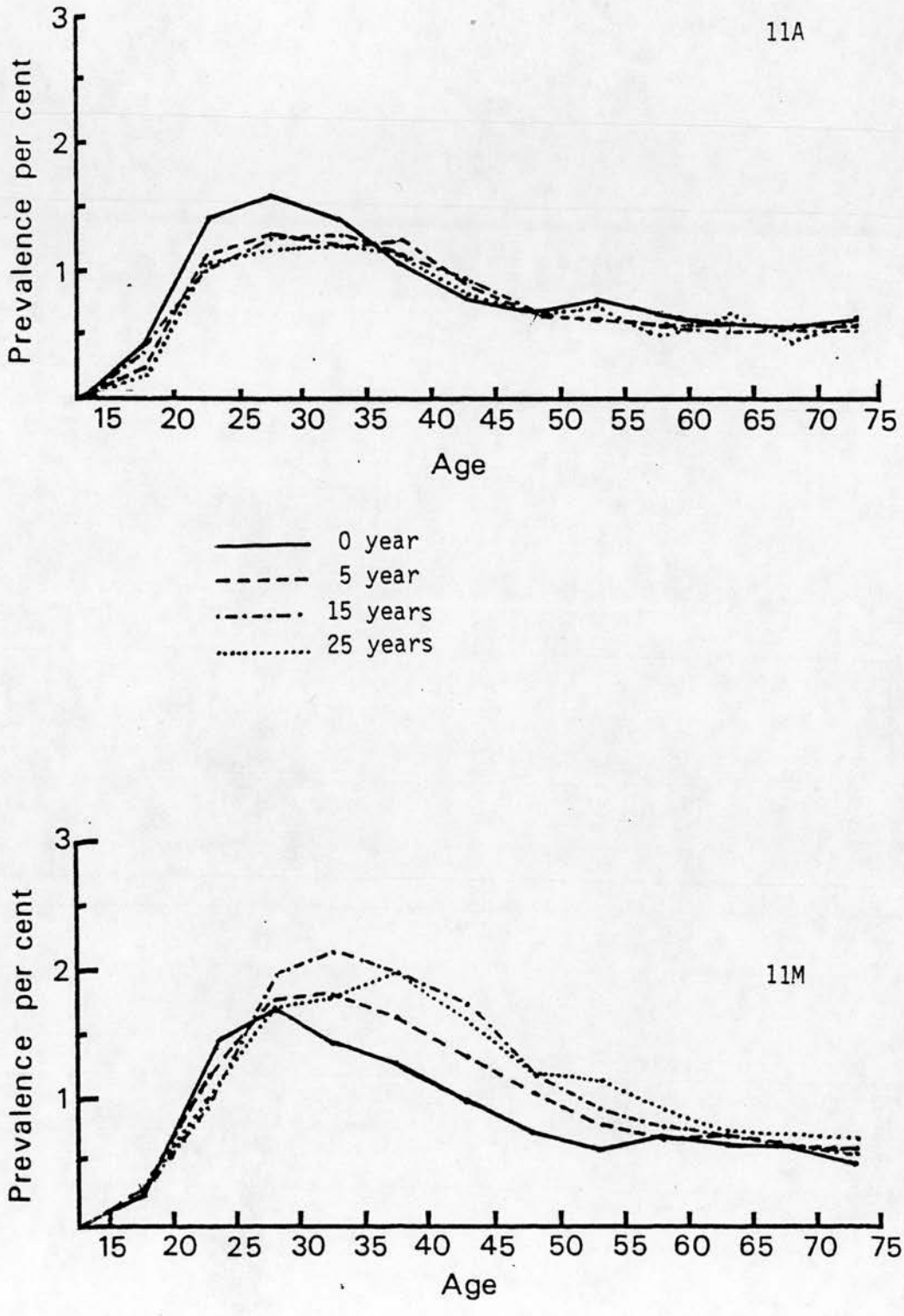


PARITY OF MARRIED FEMALES

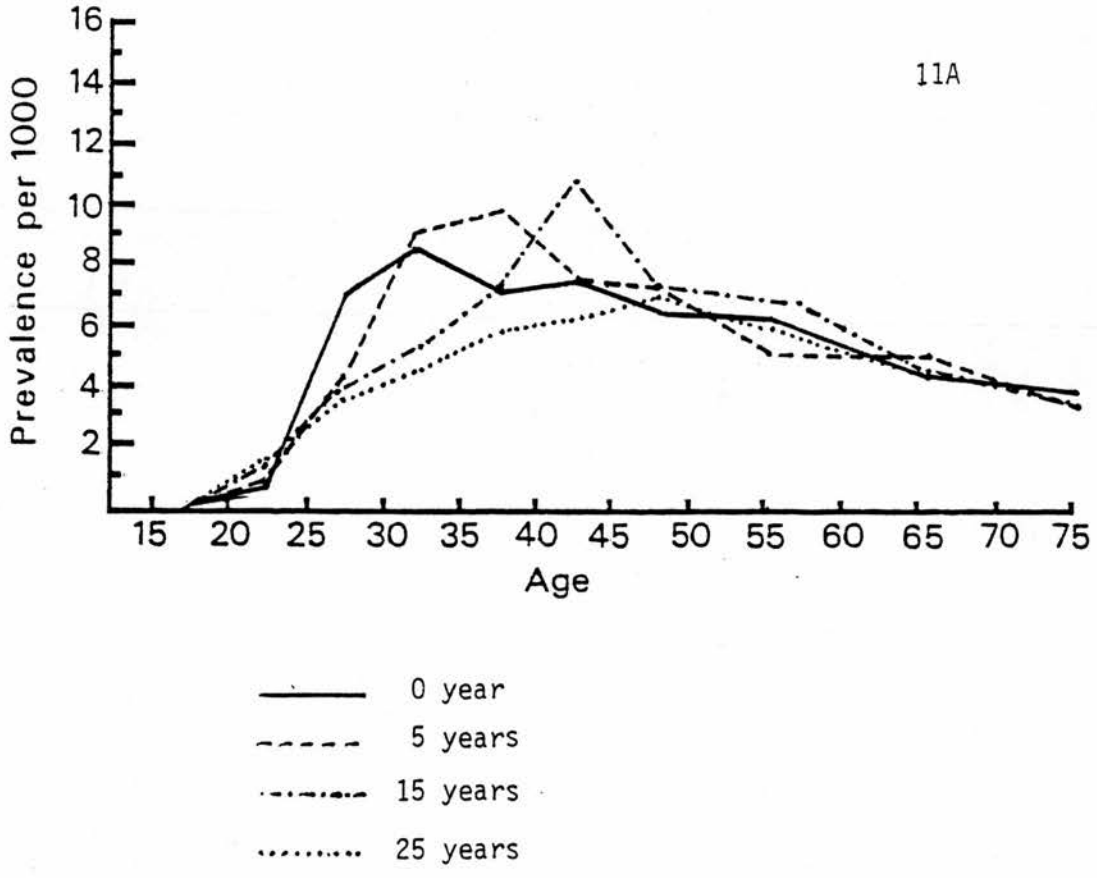
LHS : model prediction
RHS : census data (1961,1971)
GHS 80/82 (1981)


0 year
5 years
15 years
25 years
Prevalence (percent)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85
Age

ig 5.5 Prevalence of Dysplasia at different periods of simulation



ig 5.6 Prevalence of cis at different periods of simulation



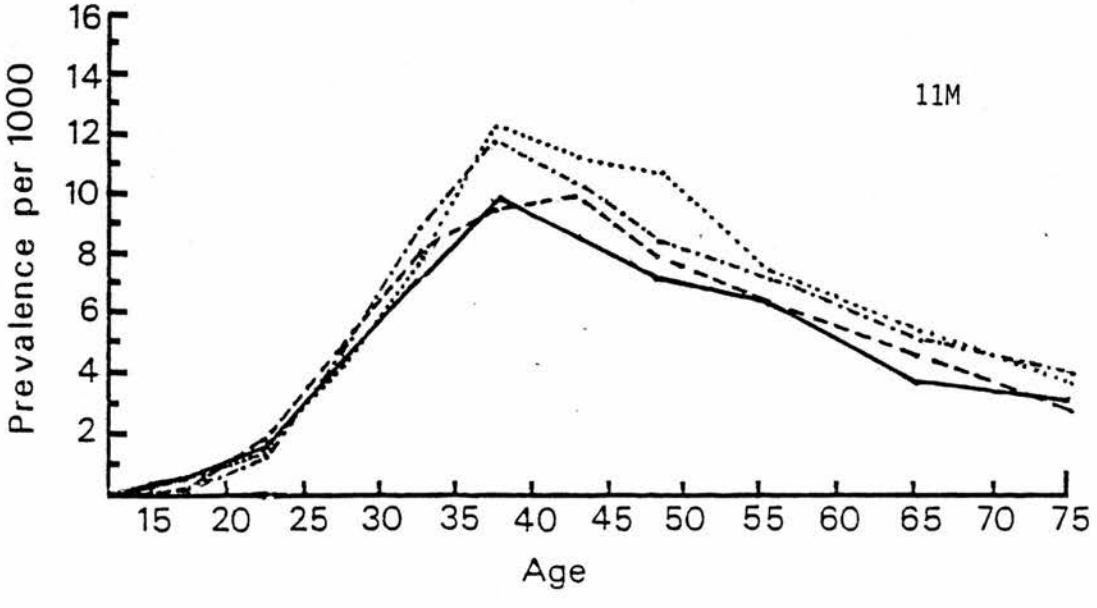


Fig 5.7

OBSERVED AND PREDICTED CLINICAL CANCER INCIDENCE

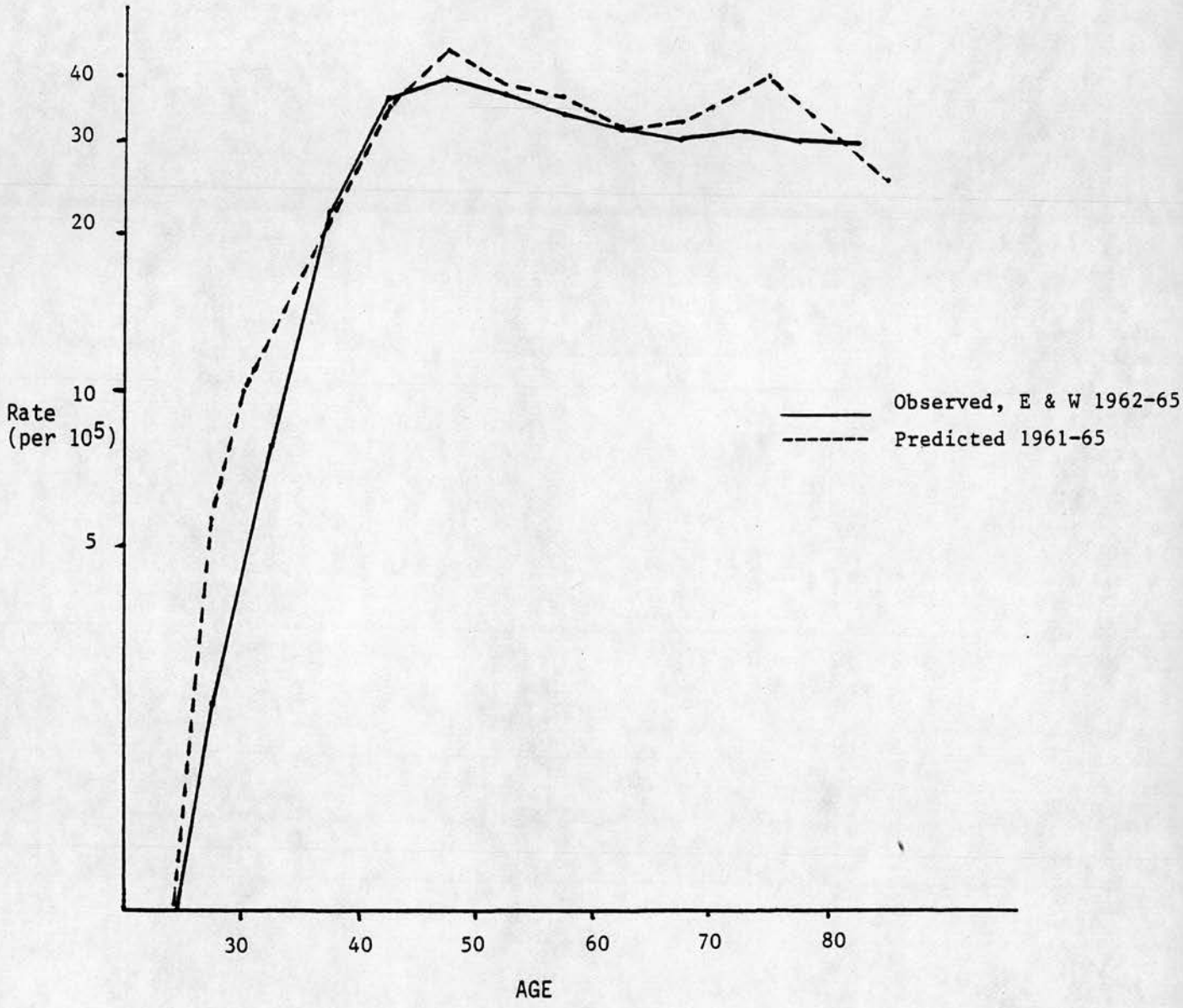


Fig 5.8 Simulated incidence and mortality of cervix cancer (no screening) 1961-1990

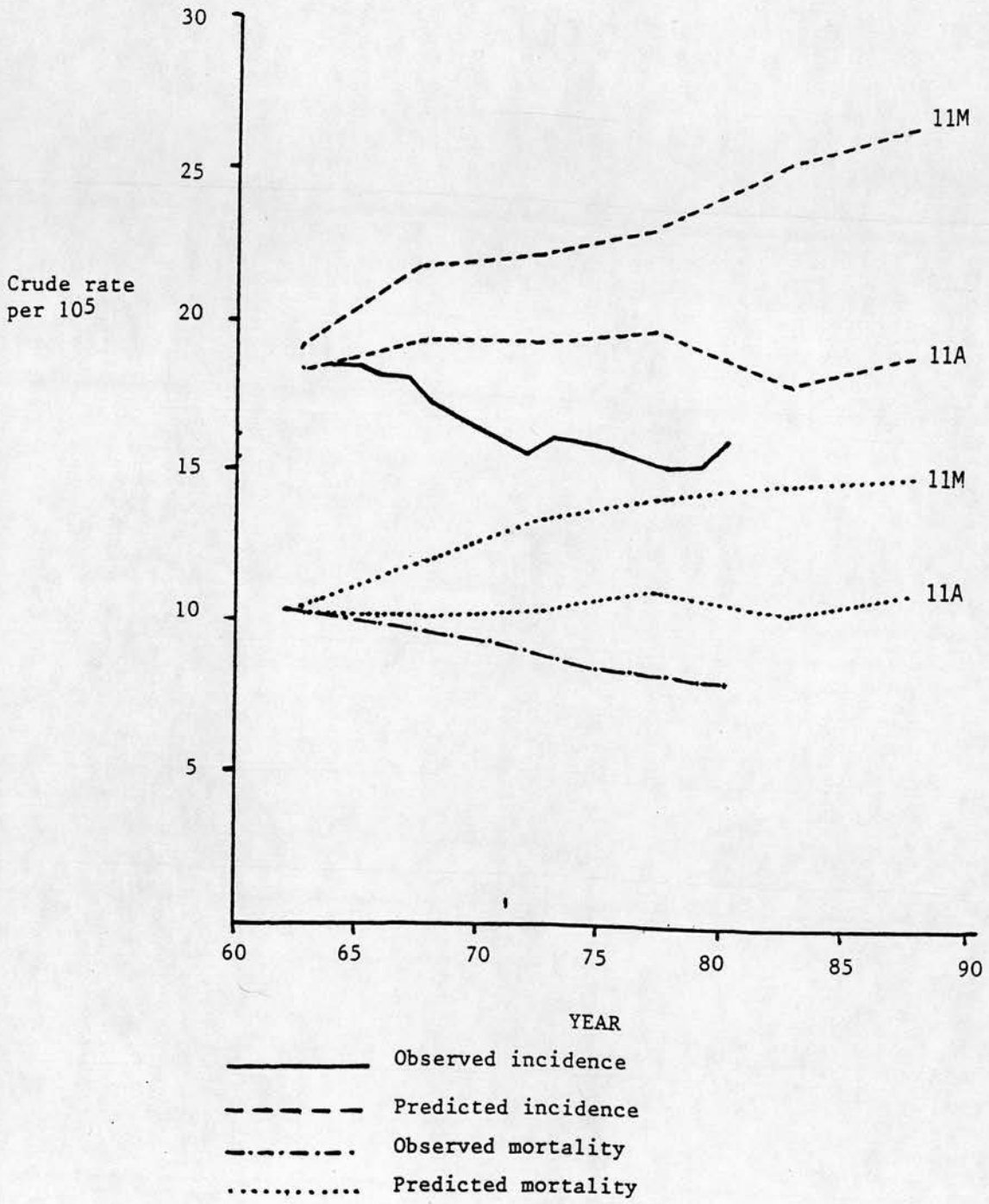


Fig 5.9 Cumulative life-years lost, screened vs unscreened, 3 natural histories

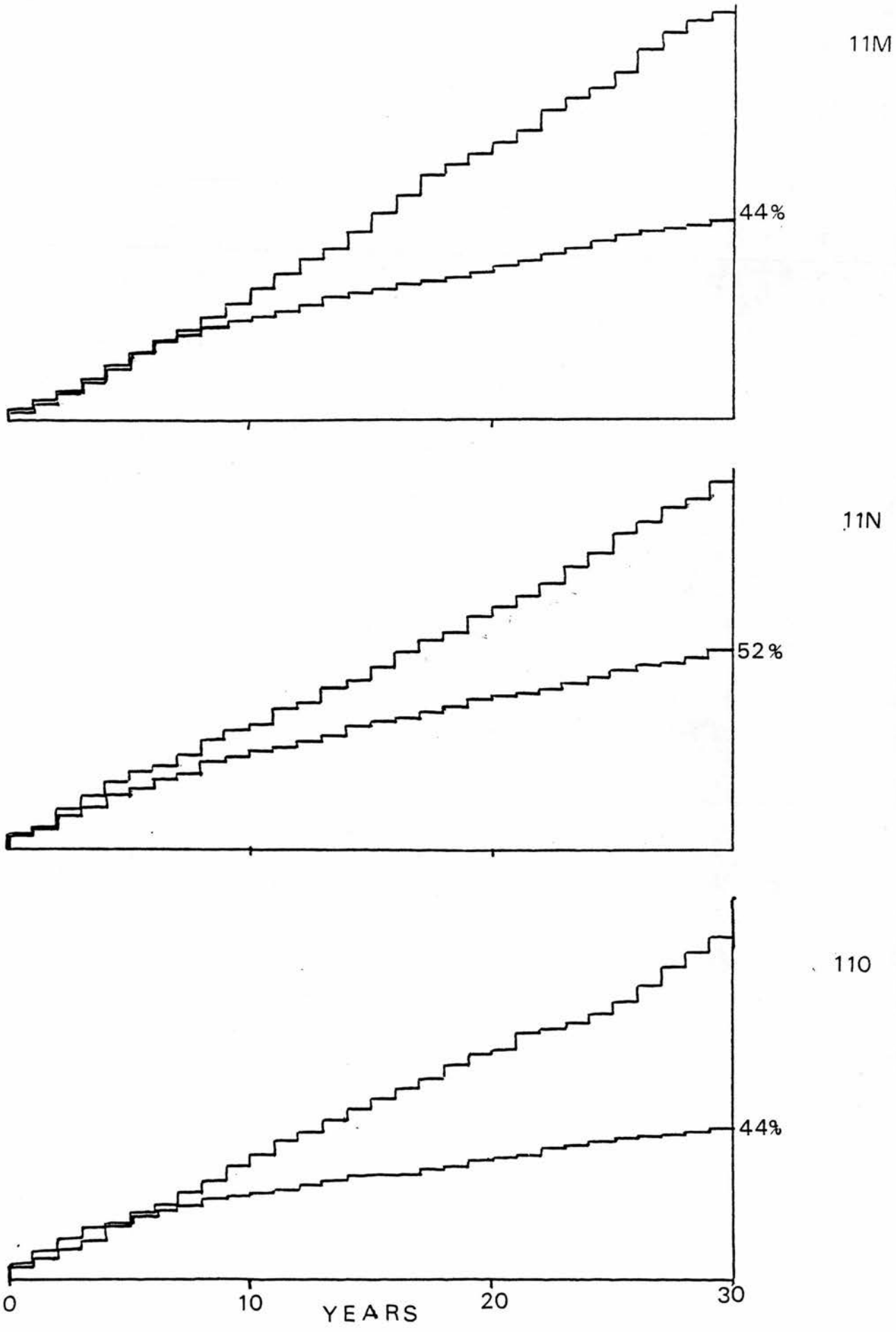


Fig 5.10 30 years screening (35-65) at different attendance rates

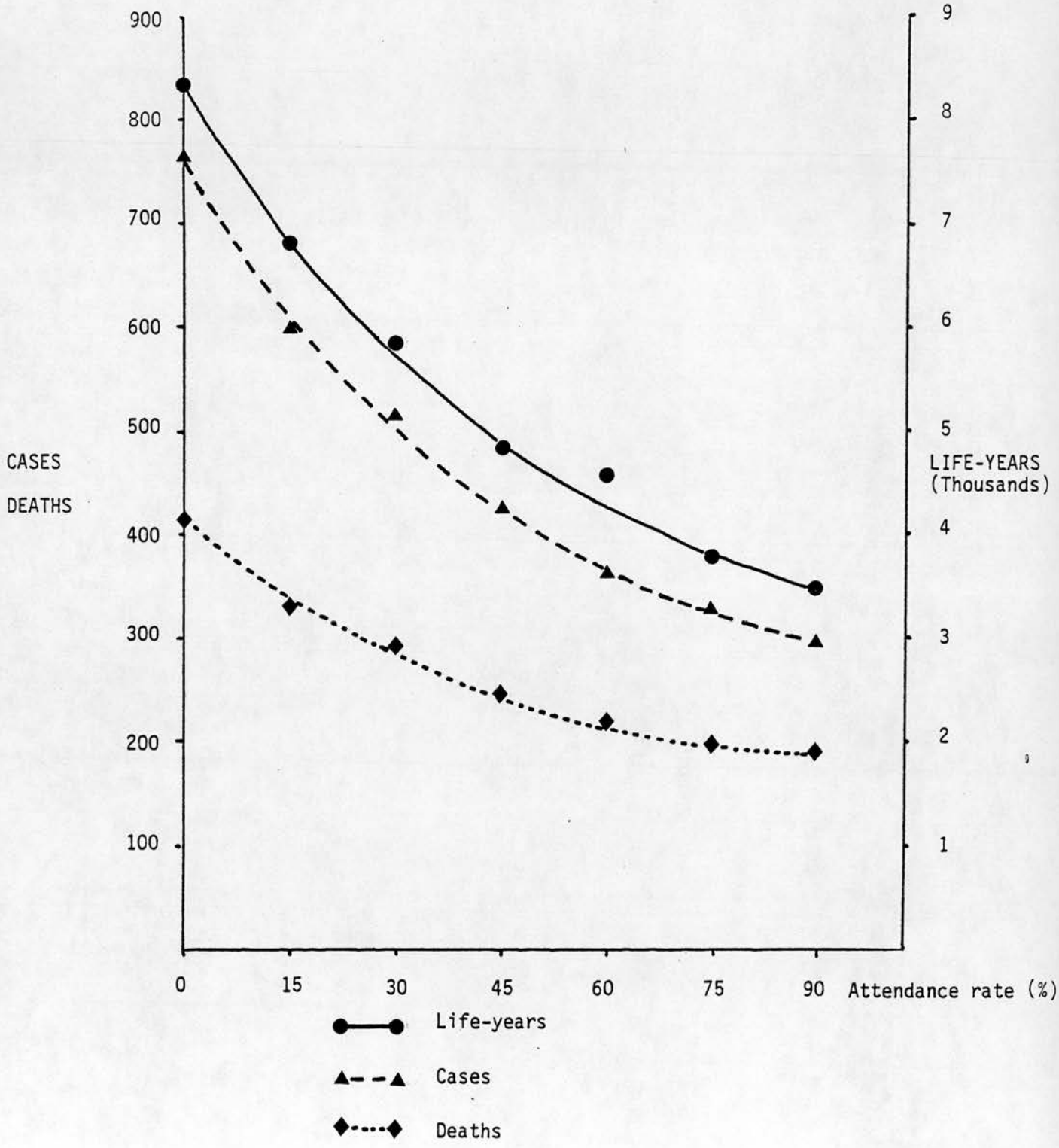
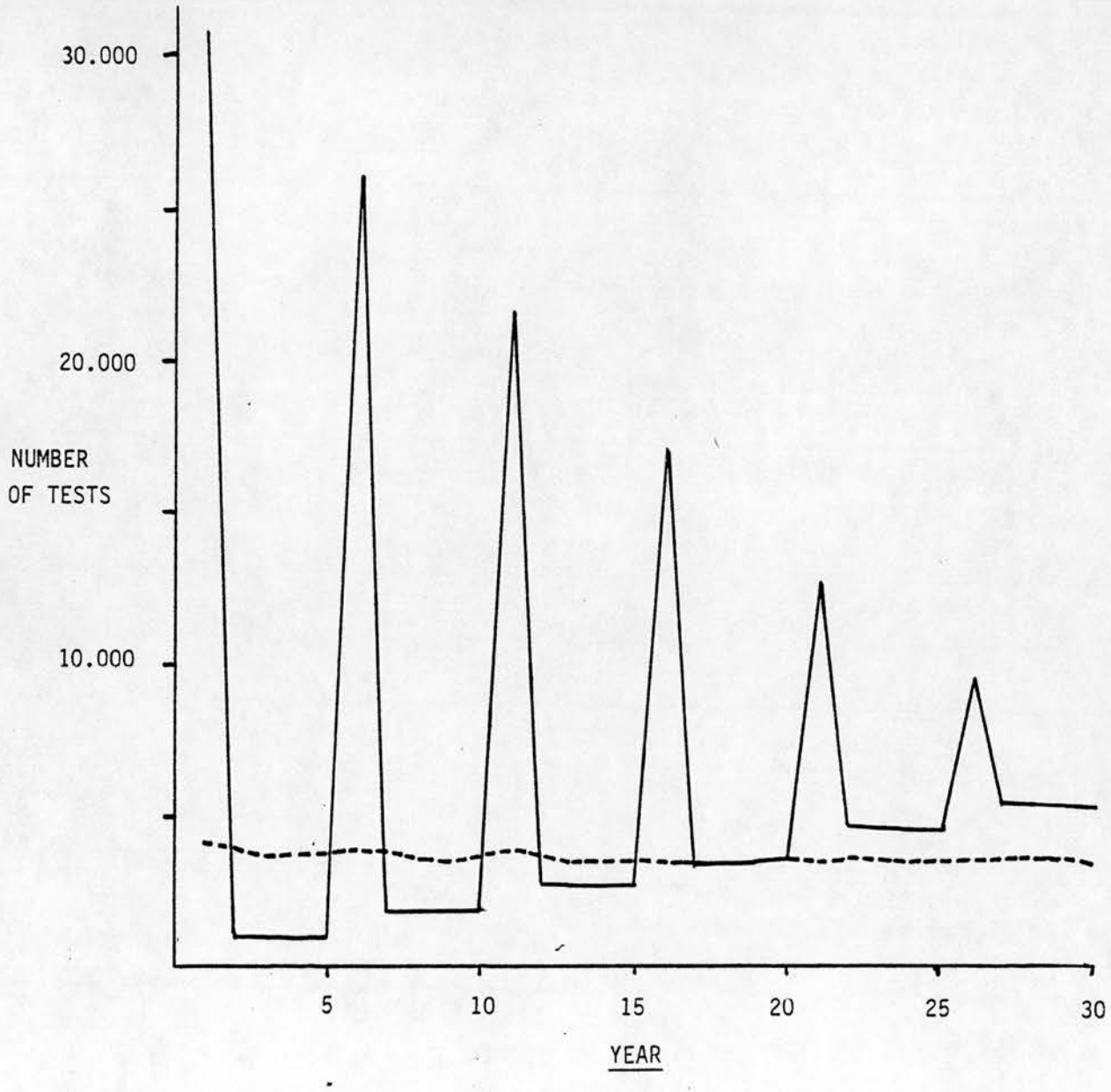


Fig 5.11 Annual numbers of tests, alternative schedules for five-yearly examinations



APPENDIX 1

GENMAK

GENMAK is a generalised markov simulation model which is deterministic in type. It examines events in a cohort of 100,000 individuals as they age from 0 to 85 years. Several versions of this are available, offering various degrees of refinement in specification of input and output.

GM.FOR is the simplest programme. In this, transfer rates between states are specified simply by age.

GMT.FOR allows duration or Time in starting state to be specified in addition.

GMTO.FOR prints a fuller output of data, producing a variety of files fully described in Appendix 3.

Attached: GMTO.FOR

```
VAX/VMS  PARKIN        GMTO 12-OCT-1983 07:39   LPAO: 12-OCT-1983 07:39   D
VAX/VMS  PARKIN        GMTO 12-OCT-1983 07:39   LPAO: 12-OCT-1983 07:39   D
VAX/VMS  PARKIN        GMTO 12-OCT-1983 07:39   LPAO: 12-OCT-1983 07:39   D
```

```
PPPP     AAA   RRRR   K   K   III   N   N
P   P   A   A  R   R  K   K   I    NN  N
P   P   A   A  R   R  K  K    I    N N N
PPPP    A   A  RRRR   KKK     I    N  NN
P       AAAAA  R R    K  K    I    N   N
P       A   A  R  R   K   K   I    N   N
P       A   A  R   R  K   K  III   N   N
```

```
  GGGGGGGG  MM       MM  TTTTTTTTTT     000000
  GGGGGGGG  MM       MM  TTTTTTTTTT     000000
GG          MMMM   MMMM      TT        00    00
GG          MMMM   MMMM      TT        00    00
GG          MM MM MM MM      TT        00    00
GG          MM  MMM  MM      TT        00    00
GG          MM   M   MM      TT        00    00
GG          MM       MM      TT        00    00
GG  GGGGGG  MM       MM      TT        00    00
GG  GGGGGG  MM       MM      TT        00    00
GG      GG  MM       MM      TT        00    00      ....
GG      GG  MM       MM      TT        00    00      ....
  GGGGGG    MM       MM      TT          000000      ....
  GGGGGG    MM       MM      TT          000000      ....
```

```
FFFFFFFFFF    000000    RRRRRRRR       ;;;;    77777777
FFFFFFFFFF    000000    RRRRRRRR       ;;;;    77777777
FF          00    00  RR      RR       ;;;;          77
FF          00    00  RR      RR       ;;;;          77
FF          00    00  RR      RR                     77
FF          00    00  RR      RR                     77
FFFFFFFF    00    00  RRRRRRRR       ;;;;        77
FFFFFFFF    00    00  RRRRRRRR       ;;;;        77
FF          00    00  RR  RR         ;;;;      77
FF          00    00  RR  RR         ;;;;      77
FF          00    00  RR    RR         ;;    77
FF          00    00  RR    RR         ;;    77
FF            000000    RR      RR     ;;    77
FF            000000    RR      RR     ;;    77
```

```
PPPP     AAA   RRRR   K   K   III   N   N
P   P   A   A  R   R  K   K   I    NN  N
P   P   A   A  R   R  K  K    I    N N N
PPPP    A   A  RRRR   KKK     I    N  NN
P       AAAAA  R R    K  K    I    N   N
P       A   A  R  R   K   K   I    N   N
P       A   A  R   R  K   K  III   N   N
```

```
VAX/VMS  PARKIN        GMTO 12-OCT-1983 07:39   LPAO: 12-OCT-1983 07:39   D
VAX/VMS  PARKIN        GMTO 12-OCT-1983 07:39   LPAO: 12-OCT-1983 07:39   D
VAX/VMS  PARKIN        GMTO 12-OCT-1983 07:39   LPAO: 12-OCT-1983 07:39   D
```

```
C-----------------------------------------------------------------------
C*****                  * * *   G M T O   * * *
C*****
C*****       A GENERAL AGE/DURATION-BASED MARKOV SIMULATION MODEL
C*****
C*****       WRITTEN BY DMP
C*****
C*****    Input via channel 1
C*****    Output to channel 6(INTERACTIVE)
C*****              channel  82 = sojourn distribution of state 2
C*****              channel  83 =    "          "          "   3
C*****              channel  92 = age/duration array of state 2(for i.p. to
C*****              channel  93 =      "          "       "    3   "    "
C-----------------------------------------------------------------------
      INTEGER VALIDTR(20,20),MORT(100),IFROM(200),INTO(200)
      REAL RATE(200)
      DIMENSION LINE(80),IMNAGE(200),IMXAGE(200)
      DIMENSION IMINDUR(200),IMAXDUR(200)
      DIMENSION POPN(21,100),POP2(21,100),XMORT(100),HYST(100)
      DIMENSION IHYST(100),POPPR(21)
      DIMENSION TRANS(100)
      DIMENSION DURST(21,100),CTMAT(21,100)
      DIMENSION TFACT(21)
      DIMENSION IASDMAT(85,21,100)
      CHARACTER*32 NAME(21)
      DATA ISLASH/''/',NAME/21*'DEAD OF OTHER CAUSE'/
C-----------------------------------------------------------------------
C*****
C*****     THIS IS THE DATA INITIALISTION SECTION
C*****
C-----------------------------------------------------------------------
      WRITE(6,500)
      READ (1,501) NUMST
  501 FORMAT(I3)
      IF(NUMST.LT.20.AND.NUMST.GT.1) GOTO 50
      WRITE(6,601) NUMST
  601 FORMAT(/'   *** INCORRECT NUMBER OF STATES --',I4,
     1' ***'/)
      STOP
   50 DO 52 I=1,NUMST
          READ(1,506) NAME(I)
   52     CONTINUE
  506 FORMAT(32A)
      READ(1,502) MORT,IHYST
      DO 53 I=1,100
          XMORT(I)=FLOAT(MORT (I))/100000.0
          HYST (I)=FLOAT(IHYST(I))/100000.0
   53     CONTINUE
      TOTST=NUMST+1
      DO 55 I=1,TOTST
          DO 55 J=1,TOTST
              VALIDTR(I,J)=0
              CONTINUE
   55     CONTINUE
      ILINE=0
  502 FORMAT(10I6)
   60 READ(1,503) LINE
  503 FORMAT(80A1)
      IF (LINE(1).EQ.ISLASH) GOTO 100
      ILINE=ILINE+1
      BACKSPACE 1
```

```
      READ(1,504) IFR,ITO
  504 FORMAT(2I3)
      IF(IFR.GE.1.AND.IFR.LT.NUMST.AND.
     1    ITO.GE.1.AND.ITO.LE.NUMST.AND.
     2    VALIDTR(IFR,ITO).EQ.0)                GOTO 80
      WRITE(6,602) ILINE
  602 FORMAT(//'    *** INCORRECT TRANSFER DEFINED IN LINE --',I4,
     1' ***'/)
      GOTO 60
   80 VALIDTR(IFR,ITO)=1
      GOTO 60
  100 ILINE=0
      NUMTR=0
   90 READ(1,503) LINE
      IF (LINE(1).EQ.ISLASH) GOTO 200
      ILINE=ILINE+1
      BACKSPACE 1
      READ(1,505) IFR,ITO,IFRAGE,ITOAGE,IFRDUR,ITODUR,RAT
      IF(IFR.GE.1.AND.IFR.LT.NUMST.AND.
     1    ITO.GE.1.AND.ITO.LE.NUMST.AND.
     2    VALIDTR(IFR,ITO).EQ.1)               GOTO 140
      WRITE(6,603) ILINE
  603 FORMAT(//'    *** INCORRECT RATE IN LINE',I4,
     1' OF TRANSFER RATES ***'/)
      WRITE(6,*) IFR,ITO,IFRAGE,ITOAGE,RAT,VALIDTR(IFR,ITO)
      GOTO 90
  140 NUMTR=NUMTR+1
      RATE  (NUMTR) = RAT
      IFROM (NUMTR) = IFR
      INTO  (NUMTR) = ITO
      IMNAGE(NUMTR) = IFRAGE
      IMXAGE(NUMTR) = ITOAGE
      IMINDUR(NUMTR) = IFRDUR
      IMAXDUR(NUMTR) = ITODUR
      GOTO 90
C-------------------------------------------------------------------------
C*****
C*****      THE SIMULATION PART STARTS HERE
C*****
C-------------------------------------------------------------------------
  200 POPN(1,1)=100000.0
      LIVST=NUMST-1
      DIST =LIVST-1
      DO 210 I=2,TOTST
        DO 210 J=1,100
          POPN(I,J)=0.0
  210     CONTINUE
      DO 450 IYR=1,85
          DO 220 I=1,TOTST
            DO 220 J=1,100
             POP2(I,J)=POPN(I,J)
  220         CONTINUE
          DO 230 I=1,LIVST
            DO 230 J=1,IYR
              POP2(TOTST,J)=POP2(TOTST,J)+POPN(I,J)*XMORT(IYR)
              POP2(I,J)     =POP2(I,J)     -POPN(I,J)*XMORT(IYR)
              IF(I.EQ.LIVST) GOTO 230
              HYSTS       =POPN(I,J)     *HYST(IYR)
              POP2(I,J)     =POP2(I,J)     -HYSTS
              POP2(LIVST,J)=POP2(LIVST,J)+HYSTS
  230         CONTINUE
```

```
            DO 300 I=1,NUMTR
              IF(IYR.LT.IMNAGE(I))  GOTO 300
              IF(IYR.GT.IMXAGE(I))  GOTO 300
                DO 250 J=IMINDUR(I),IMAXDUR(I)
                  TRANS(J) = (POPN(IFROM(I),J)*RATE(I)) / 100.0
C~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
C      INCREMENT DURATION IN STATE MATRIX FOR THIS YEAR(IYR)
C~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
             DURST(IFROM(I),J) = DURST(IFROM(I),J) + TRANS(J)
                  POP2(IFROM(I),J)=POP2(IFROM(I),J)-TRANS(J)
                  POP2(INTO (I),1)=POP2(INTO (I),1)+TRANS(J)
  250             CONTINUE
  300           CONTINUE
            DO 320 I=1,TOTST
            POPPR(I) = 0.0
            DO 320 J=1,IYR
              POPN(I,J) = POP2(I,J)
              POPPR(I) = POPPR(I) + POPN(I,J)
  320               CONTINUE
           DO 330 I = 1,TOTST
            IF(POPPR(I).NE.0.) GOTO 322
            TFACT(I) = 0.0
            GO TO 324
  322       TFACT(I) = 100/POPPR(I)
  324        CTMAT(I,1) = POPN(I,1) * TFACT(I)
             DO 330 J = 2,100
             CTMAT(I,J) = CTMAT(I,J-1) + (POPN(I,J) * TFACT(I))
             IASDMAT(IYR,I,J) = IFIX(CTMAT(I,J)+0.5)
  330        CONTINUE
           WRITE(6,606) IYR,(IFIX(POPPR(I)+0.5),I=1,TOTST)
            DO 350 I=1,TOTST
              DO 340 J=IYR,1,-1
                K=J+1
                POPN(I,K) = POPN(I,J)
  340           CONTINUE
                POPN(I,1) = 0.0
  350       CONTINUE
  450       CONTINUE
C-------------------------------------------------------------------------
C       WRITE OUTPUT FILES HERE
C-------------------------------------------------------------------------
       WRITE(82,*)(DURST(2,J),J=1,75)
       WRITE(83,*)(DURST(3,J),J=1,75)
       DO 460 IYR = 15,85
        WRITE(92,510)IYR,(IASDMAT(IYR,2,J),J=2,76)
        WRITE(93,510)IYR,(IASDMAT(IYR,3,J),J=2,76)
  460  CONTINUE
  500  FORMAT(/////10X,'G M T  - AGE/DUR MARKOV SIMULATION MODEL'
     1            /10X,'======   ------------------------------'///)
  505  FORMAT(6I3,F6.2)
  510  FORMAT(1X,I3,25I3,/,4X,25I3,/,4X,25I3)
  606      FORMAT(I4,21I6)
       END
```

APPENDIX 2

Derivation of starting prevalence data

The full date file (FILE4.DAT) for distributing the starting population into different disease states is shown in the input files in Appendix 5. It is derived from the simple prevalence rates shown in Tables IV.13 as described below.

Prevalence of the live abnormal states (2-5) in the starting population is contained in FICHE4.DAT as prevalence in 5-year age-groups per 10,000 population. Using this as input the program CRESTPRV.FOR produces the full data set of FILE4.DAT. The relative prevalence of the different states by marital state and parity as contained in the data-block of CRESTPRV is derived from Table IV.15.

The other data used is the age-marital state-parity composition of the starting population, which is read in from FOR042.

Attached:

CRESTPRV.FOR
FICHE4.DAT
FOR042

VAX/VMS PARKIN FICHE4 12-OCT-1983 07:44 LPA0: 12-OCT-1983 07:44
VAX/VMS PARKIN FICHE4 12-OCT-1983 07:44 LPA0: 12-OCT-1983 07:44
VAX/VMS PARKIN FICHE4 12-OCT-1983 07:44 LPA0: 12-OCT-1983 07:44

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K   III   N   N

FFFFFFFFFF     IIIIII       CCCCCCCC  HH       HH  EEEEEEEEEE  44     44
FFFFFFFFFF     IIIIII       CCCCCCCC  HH       HH  EEEEEEEEEE  44     44
FF               II       CC          HH       HH  EE          44     44
FF               II       CC          HH       HH  EE          44     44
FF               II       CC          HH       HH  EE          44     44
FF               II       CC          HH       HH  EE          44     44
FFFFFFFF         II       CC          HHHHHHHHHH   EEEEEEEE    4444444444
FFFFFFFF         II       CC          HHHHHHHHHH   EEEEEEEE    4444444444
FF               II       CC          HH       HH  EE              44
FF               II       CC          HH       HH  EE              44
FF               II       CC          HH       HH  EE              44
FF               II       CC          HH       HH  EE              44
FF             IIIIII       CCCCCCCC  HH       HH  EEEEEEEEEE      44
FF             IIIIII       CCCCCCCC  HH       HH  EEEEEEEEEE      44

DDDDDDDD       AAAAAA     TTTTTTTTTT      ;;;;     44     44
DDDDDDDD       AAAAAA     TTTTTTTTTT      ;;;;     44     44
DD       DD   AA    AA       TT           ;;;;     44     44
DD       DD   AA    AA       TT           ;;;;     44     44
DD       DD   AA    AA       TT                    44     44
DD       DD   AA    AA       TT                    44     44
DD       DD   AA    AA       TT           ;;;;     4444444444
DD       DD   AA    AA       TT           ;;;;     4444444444
DD       DD   AAAAAAAAAA     TT           ;;;;          44
DD       DD   AAAAAAAAAA     TT           ;;;;          44
DD       DD   AA    AA       TT             ;;          44
DD       DD   AA    AA       TT             ;;          44
DDDDDDDD      AA    AA       TT           ;;            44
DDDDDDDD      AA    AA       TT           ;;            44

PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K   III   N   N
```

VAX/VMS PARKIN FICHE4 12-OCT-1983 07:44 LPA0: 12-OCT-1983 07:44
VAX/VMS PARKIN FICHE4 12-OCT-1983 07:44 LPA0: 12-OCT-1983 07:44
VAX/VMS PARKIN FICHE4 12-OCT-1983 07:44 LPA0: 12-OCT-1983 07:44

0	0	0	0
0	0	0	0
0	0	0	0
40	3	0	0
120	18	0	0
147	49	1	1
130	76	3	2
108	90	5	8
88	88	8	15
67	79	9	20
61	68	10	22
60	58	9	21
59	51	8	20
58	45	8	18
57	40	7	17
56	36	7	14
55	33	7	12
54	30	6	10
53	28	6	10
52	26	6	10

```
PPPP     AAA   RRRR   K   K   III   N   N
P   P   A   A  R   R  K   K   I    N   N
P   P   A   A  R   R  K  K    I    NN  N
PPPP    A   A  RRRR   KKK     I    N N N
P       AAAAA  R R    K  K    I    N  NN
P       A   A  R  R   K   K   I    N   N
P       A   A  R   R  K   K  III   N   N
```

```
  CCCCCCCC  RRRRRRRR    EEEEEEEEEE    SSSSSSSS  TTTTTTTTTT  PPPPPPPP    RRRRRRRR    VV        VV
  CCCCCCCC  RRRRRRRR    EEEEEEEEEE    SSSSSSSS  TTTTTTTTTT  PPPPPPPP    RRRRRRRR    VV        VV
CC          RR      RR  EE          SS              TT      PP      PP  RR      RR  VV        VV
CC          RR      RR  EE          SS              TT      PP      PP  RR      RR  VV        VV
CC          RR      RR  EE          SS              TT      PP      PP  RR      RR  VV        VV
CC          RR      RR  EE          SS              TT      PP      PP  RR      RR  VV        VV
CC          RRRRRRRR    EEEEEEEE      SSSSSS        TT      PPPPPPPP    RRRRRRRR    VV        VV
CC          RRRRRRRR    EEEEEEEE      SSSSSS        TT      PPPPPPPP    RRRRRRRR    VV        VV
CC          RR  RR      EE                  SS      TT      PP          RR  RR      VV        VV
CC          RR  RR      EE                  SS      TT      PP          RR  RR      VV        VV
CC          RR    RR    EE                  SS      TT      PP          RR    RR      VV  VV      ....
CC          RR    RR    EE                  SS      TT      PP          RR    RR      VV  VV      ....
  CCCCCCCC  RR      RR  EEEEEEEEEE  SSSSSSSS        TT      PP          RR      RR      VV        ....
  CCCCCCCC  RR      RR  EEEEEEEEEE  SSSSSSSS        TT      PP          RR      RR      VV        ....
```

```
FFFFFFFFFF    000000    RRRRRRRR      ;;;;      333333      11
FFFFFFFFFF    000000    RRRRRRRR      ;;;;      333333      11
FF          00      00  RR      RR    ;;;;    33      33  1111
FF          00      00  RR      RR    ;;;;    33      33  1111
FF          00      00  RR      RR              33      33    11
FF          00      00  RR      RR              33      33    11
FFFFFFFF    00      00  RRRRRRRR      ;;;;        33        11
FFFFFFFF    00      00  RRRRRRRR      ;;;;        33        11
FF          00      00  RR  RR        ;;;;          33      11
FF          00      00  RR  RR        ;;;;          33      11
FF          00      00  RR    RR        ;;    33      33    11
FF          00      00  RR    RR        ;;    33      33    11
FF            000000    RR      RR      ;;      333333    111111
FF            000000    RR      RR      ;;      333333    111111
```

```
C*************************************************************************
C******  THIS PROGRAM TAKES STARTING PREVALENCE RATES OF STATES BY AGE GROU
C******   THESE ARE IN FORMAT OF FICHE4.DAT READ IN FROM FOR041
C******  DATA IS: AGE/M.S./PARITY OF STARTING POPULATION IN FOR042
C******           PREVALENCE RATIOS FOR STATES(SEE DATA IN PROGRAM)
C******           NUMBER OF ABNORMAL STATES IN FICHE4.DAT (MAX.=8)
C******  OUTPUT IS FULL PREVALENCE FILE  FILE4.DAT IN FOR043
C*************************************************************************
      DIMENSION IPOP(3,3,100)
      DIMENSION IRR(3,3,8)
      DIMENSION IPREV(20,8)
      DIMENSION ITOTPOP(100)
      DIMENSION FACT(100,8)
      DIMENSION IWR(100,8)
      DIMENSION WT(100,8)
      DIMENSION IFINR(3,3,100,8)
      DIMENSION INORMR(3,3,100)
C-------------------------------------------------------------------------
C  DATA FOR IST IS NO. OF ABNORMAL STATES IN FICHE4.DAT
C-------------------------------------------------------------------------
      DATA IST/4/
C-------------------------------------------------------------------------
C  DATA BELOW ARE RELATIVE PREVALENCE OF STATES 2...8 (PARA/M.S.)
C-------------------------------------------------------------------------
      DATA IRR/084,088,094,090,095,101,145,158,167,
     1         084,088,094,090,095,101,145,158,167,
     2         084,088,094,090,095,101,145,158,167,
     3         084,088,094,090,095,101,145,158,167,
     4         084,088,094,090,095,101,145,158,167,
     5         084,088,094,090,095,101,145,158,167,
     6         084,088,094,090,095,101,145,158,167,
     7         084,088,094,090,095,101,145,158,167/
C-------------------------------------------------------------------------
      READ(42,100)IPOP
      DO 5 N=1,20
    5   READ(41,101)(IPREV(N,S),S=1,IST)
       DO 60 S=1,IST
        DO 55 A=1,100
        ITOTPOP(A)=0
        WT(A,S)=0.0
         DO 15 M=1,3
          DO 15 P=1,3
          WT(A,S)=WT(A,S)+(IPOP(P,M,A)*IRR(P,M,S))/100
          ITOTPOP(A)=ITOTPOP(A)+IPOP(P,M,A)
   15    CONTINUE
        FACT(A,S)=ITOTPOP(A)/WT(A,S)
        L=1
   25   M=L+4
        IF(A.LE.M.AND.A.GE.L)GO TO 30
        L=L+5
        GO TO 25
   30   N=M/5
        IWR(A,S)=IPREV(N,S)*FACT(A,S)
         DO 40 M=1,3
          DO 40 P=1,3
          IFINR(P,M,A,S)=(IWR(A,S)*IRR(P,M,S))/100
   40    CONTINUE
   55   CONTINUE
   60  CONTINUE
       DO 90 A=1,100
        DO 90 M=1,3
```

```
          DO 90 P=1,3
          INORMR(P,M,A)=10000
           DO 84 S=1,IST
           INORMR(P,M,A)=INORMR(P,M,A)-IFINR(P,M,A,S)
 84         CONTINUE
 90      WRITE(43,102)INORMR(P,M,A),(IFINR(P,M,A,S),S=1,IST)
100      FORMAT(1X,9I4)
101      FORMAT(1X,<IST>I3)
 102     FORMAT(1X,<IST+1>I5)
         STOP
         END
```

```
VAX/VMS  SCRATCH        FOR042 13-OCT-1983 08:26    LPAO:  13-OCT-1983 08:34
VAX/VMS  SCRATCH        FOR042 13-OCT-1983 08:26    LPAO:  13-OCT-1983 08:34
VAX/VMS  SCRATCH        FOR042 13-OCT-1983 08:26    LPAO:  13-OCT-1983 08:34
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
FFFFFFFFFF    000000    RRRRRRRR      000000    44    44      222222
FFFFFFFFFF    000000    RRRRRRRR      000000    44    44      222222
FF           00    00   RR     RR    00    00   44    44   22      22
FF           00    00   RR     RR    00    00   44    44   22      22
FF           00    00   RR     RR    00  0000   44    44           22
FF           00    00   RR     RR    00  0000   44    44           22
FFFFFFFF     00    00   RRRRRRRR    00  00 00   4444444444       22
FFFFFFFF     00    00   RRRRRRRR    00  00 00   4444444444       22
FF           00    00   RR  RR      0000   00       44        22
FF           00    00   RR  RR      0000   00       44        22
FF           00    00   RR   RR    00      00       44     22
FF           00    00   RR   RR    00      00       44     22
FF             000000    RR     RR    000000        44    2222222222
FF             000000    RR     RR    000000        44    2222222222
```

```
DDDDDDDD      AAAAAA     TTTTTTTTTT       ;;;;        11
DDDDDDDD      AAAAAA     TTTTTTTTTT       ;;;;        11
DD      DD   AA    AA       TT            ;;;;      1111
DD      DD   AA    AA       TT            ;;;;      1111
DD      DD   AA    AA       TT                        11
DD      DD   AA    AA       TT                        11
DD      DD   AA    AA       TT            ;;;;        11
DD      DD   AA    AA       TT            ;;;;        11
DD      DD   AAAAAAAAAA     TT            ;;;;        11
DD      DD   AAAAAAAAAA     TT            ;;;;        11
DD      DD   AA    AA       TT              ;;        11
DD      DD   AA    AA       TT              ;;        11
DDDDDDDD     AA    AA       TT            ;;        111111
DDDDDDDD     AA    AA       TT            ;;        111111
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
VAX/VMS  SCRATCH        FOR042 13-OCT-1983 08:26    LPAO:  13-OCT-1983 08:34
VAX/VMS  SCRATCH        FOR042 13-OCT-1983 08:26    LPAO:  13-OCT-1983 08:34
VAX/VMS  SCRATCH        FOR042 13-OCT-1983 08:26    LPAO:  13-OCT-1983 08:34
```

S			M			FM			MS
0	1	2+	0	1	2+	0	1	2+	Parity
1487	0	0	0	0	0	0	0	0	
1488	0	0	0	0	0	0	0	0	
1490	0	0	0	0	0	0	0	0	
1402	0	0	0	0	0	0	0	0	
1359	0	0	0	0	0	0	0	0	
1356	0	0	0	0	0	0	0	0	
1358	0	0	0	0	0	0	0	0	
1317	0	0	0	0	0	0	0	0	
1306	0	0	0	0	0	0	0	0	
1357	0	0	0	0	0	0	0	0	
1370	0	0	0	0	0	0	0	0	
1434	0	0	0	0	0	0	0	0	
1514	0	0	0	0	0	0	0	0	
1656	0	0	0	0	0	0	0	0	
1724	0	0	0	0	0	0	0	0	
1279	10	0	0	0	0	0	0	0	
1449	14	0	32	18	0	0	0	0	
1271	10	0	41	45	3	0	0	0	
1185	28	0	78	40	11	0	0	0	
1010	28	0	130	66	8	0	0	0	
840	24	0	193	130	31	2	1	0	
684	26	0	277	192	68	0	0	1	
518	19	0	334	255	131	1	0	0	
397	11	0	351	284	198	2	1	0	
292	14	0	319	327	246	1	2	4	
251	10	0	311	287	310	0	0	3	
177	15	0	266	303	416	2	4	1	
158	7	1	229	331	435	3	5	8	
146	10	1	198	283	496	5	1	1	
161	15	1	198	267	551	7	2	4	
142	8	1	186	296	652	2	5	5	
125	11	3	173	314	583	3	5	10	
119	13	0	170	251	613	5	6	6	
121	7	1	152	243	618	2	2	14	
126	12	1	154	291	653	3	7	11	
127	17	0	137	290	710	3	11	9	
132	21	4	147	289	728	7	12	14	
128	8	1	153	267	731	4	16	17	
102	5	3	147	290	800	8	10	14	
134	20	2	173	317	854	8	12	23	
146	18	0	182	334	913	7	9	36	
148	10	1	157	302	834	16	35	36	
95	9	0	131	248	625	3	9	25	
90	9	0	148	228	563	6	10	26	
115	12	0	131	258	627	12	26	26	
108	14	1	154	265	632	20	23	26	
133	13	1	181	299	699	17	28	45	
121	13	2	190	288	675	15	26	50	
139	11	1	219	313	622	19	30	56	
134	11	1	182	283	612	18	26	50	
141	20	1	244	309	632	24	38	50	
156	15	1	213	265	569	26	31	57	
130	12	2	218	280	585	21	45	81	
167	15	0	214	285	559	26	42	69	
163	15	1	201	303	518	36	39	87	
153	16	2	226	242	487	49	43	81	
149	23	0	238	239	470	48	45	84	
143	12	0	212	259	461	41	53	101	
155	25	5	189	232	427	51	60	88	
155	9	4	182	230	434	55	57	117	
151	11	0	301	192	346	56	54	140	

165	19	1	283	173	296	51	59	138
157	15	2	229	135	283	57	61	158
141	16	2	221	121	287	60	84	150
150	9	2	217	152	260	59	95	157
156	15	0	101	138	288	60	61	196
135	11	3	92	114	305	64	75	208
126	17	1	101	113	257	70	77	193
122	11	2	104	109	230	68	69	233
122	13	3	83	90	217	75	84	224
121	12	2	91	102	181	68	90	218
109	13	0	61	57	160	69	70	213
105	14	0	92	48	190	53	72	233
95	11	1	53	58	169	83	70	233
94	7	0	57	37	128	71	78	252
91	13	2	32	40	122	57	65	209
74	6	1	46	40	101	65	66	248
79	9	0	27	29	86	59	52	222
59	11	1	28	32	94	48	64	197
62	2	0	24	16	53	54	48	193
61	10	0	22	16	56	39	51	193
52	6	0	22	16	40	27	36	191
36	6	0	14	11	41	32	27	160
52	9	0	8	8	23	21	36	137
40	3	0	7	3	15	24	32	129
28	4	0	4	9	16	27	29	103
26	4	0	2	0	15	15	20	86
19	0	0	2	1	8	13	20	61
19	1	0	2	0	5	10	21	43
11	1	0	1	2	3	6	7	35
9	0	0	3	1	4	9	6	25
6	1	0	0	2	3	3	2	20
6	1	0	1	2	2	3	5	12
2	0	0	1	0	1	3	1	12
2	0	0	0	0	1	2	0	11
2	1	0	0	0	0	1	3	3
1	0	0	0	0	2	0	1	5
0	1	0	0	0	0	2	0	1
0	0	0	0	0	0	0	1	3
0	0	0	0	0	0	0	0	1

APPENDIX 3

DERIVATION OF TRANSITION RATES

This appendix illustrates the use of GMTO, which is one of the versions of the generalised markov simulation model GENMAK, described in Appendix I. Here it is used to derive transition rates which are consistent with observations made on human populations.

It should be recalled that GMTO simulates events in a single cohort of individuals ageing from 0 to 85 years. However most of the data on incidence and prevalence of preclinical and clinical cancer is cross-sectional in nature - hence its use in a cohort model such as this is, strictly speaking, inappropriate ; this is discussed later.

The attached computer printouts illustrate some input data for GMTO, and results obtained.

INT1.DAT shows sets of transition rates between the following states :

1 Normal
2 Dysplasia
3 Carcinoma in situ
4 Micro/occult invasive
5 Clinical cancer

As a first stage, mortality (both cancer and other causes) is ignored, since we are interested in deriving rates rather than absolute numbers. Hysterectomy is included, since this removes 'at risk' subjects and hence markedly alters the results. Finally as an initial simplification, the transition from state 4 to state 5 is set at 100%, implying that micro/occult invasive disease lasts exactly 1 year.

The way in which transition rates from 1 to 2 have been derived from dysplasia incidence data has already been described in the main text.

The principal output file from the simulation is shown as OUT.DAT ; 1. The figures represent the numbers in each state at each year of age. Since no deaths are occurring, there are 100,000 at each age, and the figures can be read directly as prevalence per 100,000. Since the duration of state 4 is only one year, and all units in this state transfer to state 5 (transition rate 4 to 5 = 100%), the figures in this column should be the annual incidence of clinical cancer. The prevalence of carcinoma in situ can be estimated from the results of screening programmes (see Table IV.13) and column 3 (carcinoma in situ) should thus approximate these values. Given this prevalence distribution and the numbers which exit to state 4 every year (ie incidence of clinical cancer), an appropriate set of transition rates from state 3 to state 4 can be derived.

The figures in column 5 now represent cumulative incidence of clinical cancer. Note that these do not correspond to prevalence of clinical cancer, estimated in appendix 2, and reproduced in Table IV.13, since death from clinical cancer is proportional to age, and operates on this group in addition to normal mortality.

The transition rates which remain to be estimated are as follows :

State 2 to State 3 (transition from dysplasia to CIS)
State 2 to State 1 (regression of dysplasia to normal)
State 3 to State 2 (regression of CIS to dysplasia)

The rates used must be compatible with observed prevalence of the preclinical states, and also be consonant with such knowledge of natural history as is available (see II.2).

INT1.DAT represents a set of rates which maintain the prevalence of the disease states as shown in OUT.DAT. The full set of data is shown as 11M in Table IV.16. The choice of transition rates was governed by the wish to keep the figures for state 3 to state 2 transfers to a minimum, in accordance with the view that this condition rarely regresses spontaneously. With the low rates shown (1% per year up to age 50 and 0.5% per year thereafter), a transition rate from dysplasia to carcinoma in situ of 5% per year is sufficient to maintain the prevalence of the latter condition at the level

shown. This is probably a rather conservative figure judging by the observations on progression observed in various series (II.2.3). An alternative formulation would be to increase both of these rates, implying that carcinoma in situ is a more 'dynamic' condition, of higher incidence and regression, and hence shorter average duration. A data set with these specifications is reproduced in Table IV.17 (Data 11N).

A third set of data which reproduces the same pattern of prevalence in the output file is shown in Table IV.18 (Data 11O). In this formulation transition rates from carcinoma in situ (state 3) to invasive disease (state 4) are made dependent upon the duration of carcinoma in situ. In practice it proved impossible to find a data set depending only upon duration which could reproduce a similar prevalence pattern to that of OUT.DAT, thus duration specific rates for two age-groups (up to year 50, over year 50), have been used.

The figures for regression of dysplasia (25% under age 50, 12.5% over age 50) are determined by the other rates already estimated and the requirement to maintain the prevalence of dysplasia shown. These are reasonable estimates in the light of such data as is available from studies in human populations, and consistent with dysplastic changes in younger women being more transient in nature.

GMTO produces four other output files in addition to the age-specific prevalence of the different states shown as OUT.DAT.

Files FOR092 and FOR093 represent for dysplasia and c.i.s. respectively, cumulative distributions of duration at each individual year of age. These files are used in the initial stages of the main simulation (as FILE 92.DAT & FILE 93.DAT) to assign appropriate durations to the members of the starting population who are allocated to these two states (see Appendix 5).

Files FOR082 and FOR083 are the sojourn distributions of states 2 (dysplasia) and 3 (cis) - for those lesions which progress or regress in the course of simulation. These distributions are shown graphically for the three natural histories 11M, 11N and 11O as figures 4.4 & 4.5.

To complete the set of transfer rates for the model, an appropriate figure for transition from micro/occult invasive disease to clinical cancer is required. The duration of this state is not known, but its prevalence, when studied, has been generally much lower than carcinoma in situ. The solution adopted in the natural histories of Tables IV.16-18 is to make the duration fixed at 2 years, so that transfer rates are zero in year 1 and 100% in year 2. The result of this is a doubling of the prevalence figures for state 4 shown in OUT.DAT. The transfer rates for 5 to 8 transitions shown in the natural histories are derived from England and Wales survival data as already described (see Figure 4.3).

The final stage in creating the transition rate data file for the main model is to incorporate data on relative risk according to marital state and parity. The relevant data is shown in Table IV.15. Since the relative risk figures apply to incidence of preclinical disease (and not to transfer between different stages of preclinical disease), adjustment of crude rates is made only for transitions from normality (ie in the natural history modelled, transfer rates 1-2).

However, it is not possible to obtain age-parity-marital state specific rates directly, by applying the relative risk to the crude 1-2 transition rates in the data of tables IV.16-18 (FICHE 11.DAT). These rates were based on population observation, and are hence already weighted by the marital state and parity distribution in each of the age groups. An unweighted rate must be calculated, to which the relative risk figures can be applied.

The program CRETRAT uses the relative risk figures (as a data block within the program), the crude transfer rate data in FICHE 11.DAT and the population structure by age, marital status and parity (FORO42) to produce the full set of transition data used by the model (FILE 11.DAT). This latter incorporates a set of rates for each decade simulated to allow for changing transition rates or population structure.

The use of a single set of transition rates over the 30 year period of the simulation implies that transition rates are the same for all birth cohorts in the population. In fact, as has been described in section II, there are quite marked changes in disease risk according to year of birth. This can

be allowed for in the model by reading in new data files for different periods of simulation; in the program shown a new data set is read for each decade. The main problem concerns the decision about which transitions should be changed to correspond to an apparent increase in incidence of invasive cancer - is this the end result of a rise in probability of the first step in the natural history (incidence of dysplasia), or are other transitions changed as well?

If transition rates are made dependent upon individual characteristics (e.g. marital state and/or parity) a secular change in the distribution of these variables in the population will give rise to changes in disease rates. Care must be taken therefore that any ad-hoc increase in transition rates designed to simulate cohort effects represent residual changes after those attributable to personal variables are taken into account.

Attached

INT1.DAT
OUT1.DAT
FOR082
FOR083
CRETRAT.FOR

```
VAX/VMS  PARKIN        INT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:00   US:
VAX/VMS  PARKIN        INT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:00   US:
VAX/VMS  PARKIN        INT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:00   US:
```

```
PPPP     AAA   RRRR   K   K   III   N   N
P   P   A   A  R   R  K   K    I    N   N
P   P   A   A  R   R  K  K     I    NN  N
PPPP    A   A  RRRR   KKK      I    N N N
P       AAAAA  R R    K  K     I    N  NN
P       A   A  R  R   K   K    I    N   N
P       A   A  R   R  K   K   III   N   N
```

```
IIIIII     NN       NN  TTTTTTTTTT      11
IIIIII     NN       NN  TTTTTTTTTT      11
  II       NN       NN      TT        1111
  II       NN       NN      TT        1111
  II       NNNN     NN      TT          11
  II       NNNN     NN      TT          11
  II       NN  NN   NN      TT          11
  II       NN  NN   NN      TT          11
  II       NN    NNNN      TT          11
  II       NN    NNNN      TT          11
  II       NN      NN      TT          11          ....
  II       NN      NN      TT          11          ....
IIIIII     NN      NN      TT      111111          ....
IIIIII     NN      NN      TT      111111          ....
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;      333333
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;      333333
DD      DD   AA    AA      TT          ;;;;    33      33
DD      DD   AA    AA      TT          ;;;;    33      33
DD      DD   AA    AA      TT                          33
DD      DD   AA    AA      TT                          33
DD      DD   AA    AA      TT          ;;;;          33
DD      DD   AA    AA      TT          ;;;;          33
DD      DD   AAAAAAAAAA    TT          ;;;;            33
DD      DD   AAAAAAAAAA    TT          ;;;;            33
DD      DD   AA    AA      TT            ;;    33      33
DD      DD   AA    AA      TT            ;;    33      33
DDDDDDDD     AA    AA      TT          ;;        333333
DDDDDDDD     AA    AA      TT          ;;        333333
```

```
PPPP     AAA   RRRR   K   K   III   N   N
P   P   A   A  R   R  K   K    I    N   N
P   P   A   A  R   R  K  K     I    NN  N
PPPP    A   A  RRRR   KKK      I    N N N
P       AAAAA  R R    K  K     I    N  NN
P       A   A  R  R   K   K    I    N   N
P       A   A  R   R  K   K   III   N   N
```

```
VAX/VMS  PARKIN        INT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:00   US:
VAX/VMS  PARKIN        INT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:00   US:
VAX/VMS  PARKIN        INT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:00   US:
```

```
  7
NORMAL
DYSP
CIS
OCCINV
CLINCA
HYSTERECTOMY
DEAD OF CANCER
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0     0     0     0     0     0
     0     0     0     0     0    20    40    80   120   160
   220   260   300   380   460   540   620   680   740   800
   860   900   900   800   700   600   520   460   400   340
   280   220   160   156   152   148   144   140   144   148
   152   156   160   156   152   148   144   140   132   124
   116   108   100    98    96    94    92    90    88    86
    84    82    80    80    80    80    80    80    80    80
    80    80    80    80    80    80    80    80    80    80
  1  2
  2  3
  2  1
  3  2
  3  4
  4  5
//
  1  2 15 19 01 99  0.17
  1  2 20 24 01 99  0.50
  1  2 25 29 01 99  0.45
  1  2 30 34 01 99  0.37
  1  2 35 39 01 99  0.31
  1  2 40 44 01 99  0.25
  1  2 45 49 01 99  0.19
  1  2 50 85 01 99  0.12
  2  1 15 49 01 99 25.0
  2  1 50 85 01 99 12.5      !classic N.H.
  2  3 15 85 01 99  5.0      !not time dependant
  3  2 15 49 01 99  1.0
  3  2 50 85 01 99  0.5
  3  4 15 19 01 99  0.5
  3  4 20 24 01 99  1.0
  3  4 25 29 01 99  1.5
  3  4 30 34 01 99  2.0
  3  4 35 39 01 99  3.0
  3  4 40 44 01 99  5.0
  3  4 45 49 01 99  5.0
  3  4 50 59 01 99  7.0
  3  4 60 69 01 99  8.0
  3  4 70 79 01 99  9.0
  3  4 80 85 01 99 10.0
  4  5 15 85 01 99100.0
//
```

```
VAX/VMS  PARKIN        OUT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:01   US:
VAX/VMS  PARKIN        OUT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:01   US:
VAX/VMS  PARKIN        OUT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:01   US:
```

```
                    PPPP     AAA   RRRR   K   K   III   N   N
                    P   P   A   A  R   R  K   K    I    N   N
                    P   P   A   A  R   R  K  K     I    NN  N
                    PPPP    A   A  RRRR   KKK      I    N N N
                    P       AAAAA  R R    K  K     I    N  NN
                    P       A   A  R  R   K   K    I    N   N
                    P       A   A  R   R  K   K   III   N   N
```

```
  OOOOOO    UU      UU  TTTTTTTTTT      11
  OOOOOO    UU      UU  TTTTTTTTTT      11
OO      OO  UU      UU      TT        1111
OO      OO  UU      UU      TT        1111
OO      OO  UU      UU      TT          11
OO      OO  UU      UU      TT          11
OO      OO  UU      UU      TT          11
OO      OO  UU      UU      TT          11
OO      OO  UU      UU      TT          11
OO      OO  UU      UU      TT          11
OO      OO  UU      UU      TT          11          ....
OO      OO  UU      UU      TT          11          ....
  OOOOOO    UUUUUUUUUU      TT        111111        ....
  OOOOOO    UUUUUUUUUU      TT        111111        ....
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT       ;;;;       222222
DDDDDDDD      AAAAAA    TTTTTTTTTT       ;;;;       222222
DD      DD  AA      AA      TT           ;;;;     22      22
DD      DD  AA      AA      TT           ;;;;     22      22
DD      DD  AA      AA      TT                            22
DD      DD  AA      AA      TT                            22
DD      DD  AA      AA      TT           ;;;;           22
DD      DD  AA      AA      TT           ;;;;           22
DD      DD  AAAAAAAAAA      TT           ;;;;         22
DD      DD  AAAAAAAAAA      TT           ;;;;         22
DD      DD  AA      AA      TT             ;;       22
DD      DD  AA      AA      TT             ;;       22
DDDDDDDD    AA      AA      TT           ;;       2222222222
DDDDDDDD    AA      AA      TT           ;;       2222222222
```

```
                    PPPP     AAA   RRRR   K   K   III   N   N
                    P   P   A   A  R   R  K   K    I    N   N
                    P   P   A   A  R   R  K  K     I    NN  N
                    PPPP    A   A  RRRR   KKK      I    N N N
                    P       AAAAA  R R    K  K     I    N  NN
                    P       A   A  R  R   K   K    I    N   N
                    P       A   A  R   R  K   K   III   N   N
```

```
VAX/VMS  PARKIN        OUT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:01   US:
VAX/VMS  PARKIN        OUT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:01   US:
VAX/VMS  PARKIN        OUT1  8-FEB-1984 08:00   LPA0:   8-FEB-1984 08:01   US:
```

G M T - AGE/DUR MARKOV SIMULATION MODEL

1100000	0	0	0	0	0	0	0
2100000	0	0	0	0	0	0	0
3100000	0	0	0	0	0	0	0
4100000	0	0	0	0	0	0	0
5100000	0	0	0	0	0	0	0
6100000	0	0	0	0	0	0	0
7100000	0	0	0	0	0	0	0
8100000	0	0	0	0	0	0	0
9100000	0	0	0	0	0	0	0
10100000	0	0	0	0	0	0	0
11100000	0	0	0	0	0	0	0
12100000	0	0	0	0	0	0	0
13100000	0	0	0	0	0	0	0
14100000	0	0	0	0	0	0	0
15 99830	170	0	0	0	0	0	0
16 99703	289	9	0	0	0	0	0
17 99605	372	23	0	0	0	0	0
18 99529	430	41	0	0	0	0	0
19 99467	470	62	0	0	0	0	0
20 99088	827	84	1	0	0	0	0
21 98799	1075	124	1	1	0	0	0
22 98574	1248	175	1	2	0	0	0
23 98393	1368	234	2	3	0	0	0
24 98243	1452	298	2	5	0	0	0
25 98164	1462	363	4	7	0	0	0
26 98068	1468	427	5	12	20	0	0
27 97954	1473	489	6	17	60	0	0
28 97803	1475	550	7	23	140	0	0
29 97615	1477	610	8	31	260	0	0
30 97467	1399	664	12	39	419	0	0
31 97241	1343	713	13	51	638	0	0
32 96964	1304	757	14	64	897	0	0
33 96641	1275	797	15	78	1194	0	0
34 96235	1253	834	16	93	1570	0	0
35 95807	1178	859	25	108	2022	0	0
36 95287	1124	879	26	133	2551	0	0
37 94682	1084	895	26	158	3156	0	0
38 94015	1054	907	27	183	3814	0	0
39 93292	1030	917	27	208	4526	0	0
40 92570	955	906	46	233	5290	0	0
41 91781	901	892	45	277	6104	0	0
42 90951	861	875	44	319	6949	0	0
43 90120	831	858	43	361	7787	0	0
44 89382	809	841	43	401	8524	0	0
45 88789	739	825	42	441	9165	0	0
46 88272	690	808	41	480	9710	0	0
47 87817	655	789	40	519	10179	0	0
48 87410	630	771	39	556	10592	0	0
49 87052	612	753	38	593	10950	0	0
50 86728	611	725	53	630	11253	0	0
51 86458	610	699	51	681	11501	0	0

52	86240	609	676	49	730	11696	0	0
53	86075	609	654	47	777	11837	0	0
54	85913	608	635	46	823	11975	0	0
55	85756	607	617	44	868	12109	0	0
56	85602	606	600	43	911	12239	0	0
57	85452	605	584	42	953	12365	0	0
58	85305	603	570	41	993	12488	0	0
59	85155	602	556	40	1033	12614	0	0
60	85002	601	538	44	1071	12743	0	0
61	84846	599	522	43	1114	12876	0	0
62	84687	598	507	42	1155	13012	0	0
63	84524	597	493	40	1195	13151	0	0
64	84366	595	480	39	1234	13286	0	0
65	84211	594	468	38	1271	13418	0	0
66	84059	592	457	37	1307	13546	0	0
67	83911	591	447	37	1343	13671	0	0
68	83767	590	438	36	1378	13792	0	0
69	83630	588	430	35	1412	13905	0	0
70	83499	587	418	39	1445	14012	0	0
71	83375	586	407	38	1482	14112	0	0
72	83259	585	397	37	1518	14205	0	0
73	83149	584	388	36	1553	14291	0	0
74	83040	583	380	35	1587	14375	0	0
75	82934	582	373	34	1620	14457	0	0
76	82829	581	366	34	1653	14537	0	0
77	82726	580	360	33	1685	14616	0	0
78	82625	579	355	32	1717	14693	0	0
79	82525	578	350	32	1747	14768	0	0
80	82428	577	341	35	1778	14841	0	0
81	82332	576	334	34	1811	14913	0	0
82	82237	575	328	33	1844	14982	0	0
83	82145	575	322	33	1876	15050	0	0
84	82052	574	316	32	1907	15118	0	0
85	81960	573	312	32	1938	15186	0	0

```
VAX/VMS  PARKIN        FOR082  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
VAX/VMS  PARKIN        FOR082  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
VAX/VMS  PARKIN        FOR082  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K    I     N   N
P   P   A   A   R   R   K  K     I     NN  N
PPPP    A   A   RRRR    KKK      I     N N N
P       AAAAA   R R     K  K     I     N  NN
P       A   A   R  R    K   K    I     N   N
P       A   A   R   R   K   K   III    N   N
```

```
FFFFFFFFFF    000000    RRRRRRRR      000000      888888      222222
FFFFFFFFFF    000000    RRRRRRRR      000000      888888      222222
FF           00    00   RR     RR   00    00    88    88    22    22
FF           00    00   RR     RR   00    00    88    88    22    22
FF           00    00   RR     RR   00  0000    88    88          22
FF           00    00   RR     RR   00  0000    88    88          22
FFFFFFFF     00    00   RRRRRRRR    00  00 00     888888        22
FFFFFFFF     00    00   RRRRRRRR    00  00 00     888888        22
FF           00    00   RR  RR      0000  00    88    88      22
FF           00    00   RR  RR      0000  00    88    88      22
FF           00    00   RR   RR     00    00    88    88    22
FF           00    00   RR   RR     00    00    88    88    22
FF             000000    RR     RR    000000      888888    2222222222
FF             000000    RR     RR    000000      888888    2222222222
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;      333333
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;      333333
DD      DD   AA    AA      TT          ;;;;     33     33
DD      DD   AA    AA      TT          ;;;;     33     33
DD      DD   AA    AA      TT                          33
DD      DD   AA    AA      TT                          33
DD      DD   AA    AA      TT          ;;;;           33
DD      DD   AA    AA      TT          ;;;;           33
DD      DD   AAAAAAAAAA    TT          ;;;;             33
DD      DD   AAAAAAAAAA    TT          ;;;;             33
DD      DD   AA    AA      TT            ;;     33     33
DD      DD   AA    AA      TT            ;;     33     33
DDDDDDDD     AA    AA      TT          ;;       333333
DDDDDDDD     AA    AA      TT          ;;       333333
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K    I     N   N
P   P   A   A   R   R   K  K     I     NN  N
PPPP    A   A   RRRR    KKK      I     N N N
P       AAAAA   R R     K  K     I     N  NN
P       A   A   R  R    K   K    I     N   N
P       A   A   R   R   K   K   III    N   N
```

```
VAX/VMS  PARKIN        FOR082  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
VAX/VMS  PARKIN        FOR082  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
VAX/VMS  PARKIN        FOR082  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
```

0. 0000000E+00	3905. 484	2776. 849	1982. 835	1422. 473
1025. 607	742. 3264	540. 5642	396. 1298	292. 1597
216. 8742	161. 8383	121. 5696	91. 89880	69. 88165
53. 42951	41. 02259	31. 64447	24. 50981	19. 04951
14. 84795	11. 59276	9. 069077	7. 104789	5. 570880
4. 369841	3. 426750	2. 686052	2. 103639	1. 645378
1. 284737	1. 001771	0. 7788301	0. 6034525	0. 4657233
0. 3577917	0. 2734862	0. 1972003	0. 1427918	0. 1038789
7. 5958386E-02	5. 5852942E-02	3. 9896172E-02	2. 8594147E-02	2. 0575987E-02
1. 4873400E-02	1. 0805412E-02	7. 6593347E-03	5. 4439465E-03	3. 8811893E-03
2. 7767001E-03	1. 9942981E-03	1. 3998287E-03	9. 8359305E-04	6. 9190172E-04
4. 8735624E-04	3. 4382727E-04	2. 3436555E-04	1. 5890718E-04	1. 0702603E-04
7. 1467257E-05	4. 7194382E-05	2. 9795150E-05	1. 8181563E-05	1. 0516902E-05
5. 5336227E-06	2. 3593454E-06	1. 4196709E-06	8. 0278483E-07	4. 0450990E-07
1. 5325601E-07	0. 0000000E+00	0. 0000000E+00	0. 0000000E+00	0. 0000000E+00

```
VAX/VMS  PARKIN        FOR083  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
VAX/VMS  PARKIN        FOR083  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
VAX/VMS  PARKIN        FOR083  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
```

```
PPPP     AAA   RRRR   K   K   III   N   N
P   P   A   A  R   R  K   K    I    N   N
P   P   A   A  R   R  K  K     I    NN  N
PPPP    A   A  RRRR   KKK      I    N N N
P       AAAAA  R R    K  K     I    N  NN
P       A   A  R  R   K   K    I    N   N
P       A   A  R   R  K   K   III   N   N
```

```
FFFFFFFFFF    000000    RRRRRRRR      000000      888888      333333
FFFFFFFFFF    000000    RRRRRRRR      000000      888888      333333
FF           00    00   RR     RR   00    00    88    88    33    33
FF           00    00   RR     RR   00    00    88    88    33    33
FF           00    00   RR     RR   00  0000    88    88          33
FF           00    00   RR     RR   00  0000    88    88          33
FFFFFFFF     00    00   RRRRRRRR    00 00 00      888888        33
FFFFFFFF     00    00   RRRRRRRR    00 00 00      888888        33
FF           00    00   RR  RR      0000  00    88    88          33
FF           00    00   RR  RR      0000  00    88    88          33
FF           00    00   RR   RR     00    00    88    88    33    33
FF           00    00   RR   RR     00    00    88    88    33    33
FF             000000    RR     RR    000000      888888      333333
FF             000000    RR     RR    000000      888888      333333
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT       ;;;;      333333
DDDDDDDD      AAAAAA    TTTTTTTTTT       ;;;;      333333
DD      DD   AA    AA      TT           ;;;;    33      33
DD      DD   AA    AA      TT           ;;;;    33      33
DD      DD   AA    AA      TT                           33
DD      DD   AA    AA      TT                           33
DD      DD   AA    AA      TT           ;;;;          33
DD      DD   AA    AA      TT           ;;;;          33
DD      DD   AAAAAAAAAA    TT           ;;;;            33
DD      DD   AAAAAAAAAA    TT           ;;;;            33
DD      DD   AA    AA      TT             ;;    33      33
DD      DD   AA    AA      TT             ;;    33      33
DDDDDDDD     AA    AA      TT           ;;        333333
DDDDDDDD     AA    AA      TT           ;;        333333
```

```
PPPP     AAA   RRRR   K   K   III   N   N
P   P   A   A  R   R  K   K    I    N   N
P   P   A   A  R   R  K  K     I    NN  N
PPPP    A   A  RRRR   KKK      I    N N N
P       AAAAA  R R    K  K     I    N  NN
P       A   A  R  R   K   K    I    N   N
P       A   A  R   R  K   K   III   N   N
```

```
VAX/VMS  PARKIN        FOR083  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
VAX/VMS  PARKIN        FOR083  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
VAX/VMS  PARKIN        FOR083  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:01
```

0. 0000000E+00	155. 8247	145. 3460	135. 8025	127. 0880
119. 1057	111. 7578	104. 9898	98. 71976	92. 89056
87. 44585	82. 34564	77. 56727	73. 06191	68. 77806
64. 65787	60. 75817	57. 04992	53. 48262	50. 00466
46. 55110	43. 32902	40. 32079	37. 49886	34. 83326
32. 29004	29. 92156	27. 71085	25. 63456	23. 67075
21. 79453	20. 05929	18. 45296	16. 96100	15. 56868
14. 26068	13. 05545	11. 94098	10. 90519	9. 937826
9. 027861	8. 186311	7. 414917	6. 705963	6. 051867
5. 444732	4. 886579	4. 378148	3. 911556	3. 481162
3. 081043	2. 714882	2. 383431	2. 081543	1. 805125
1. 549989	1. 316409	1. 107077	0. 9188221	0. 7491250
0. 5955119	0. 4596718	0. 3434997	0. 2460758	0. 1676016
0. 1091444	7. 4901991E-02	4. 6660684E-02	2. 4415771E-02	8. 5895984E-03
0. 0000000E+00	0. 0000000E+00	0. 0000000E+00	0. 0000000E+00	0. 0000000E+00

```
/VMS  PARKIN        CRETRAT  8-FEB-1984 08:01    LPAO:   8-FEB-1984 08:02    US:[DM.SI
/VMS  PARKIN        CRETRAT  8-FEB-1984 08:01    LPAO:   8-FEB-1984 08:02    US:[DM.SI
/VMS  PARKIN        CRETRAT  8-FEB-1984 08:01    LPAO:   8-FEB-1984 08:02    US:[DM.SI
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K    III    N   N
```

```
   CCCCCCCC  RRRRRRRR     EEEEEEEEEE  TTTTTTTTTT  RRRRRRRR      AAAAAA     TTTTTTTTT
   CCCCCCCC  RRRRRRRR     EEEEEEEEEE  TTTTTTTTTT  RRRRRRRR      AAAAAA     TTTTTTTTT
 CC          RR      RR   EE              TT      RR      RR   AA      AA      TT
 CC          RR      RR   EE              TT      RR      RR   AA      AA      TT
 CC          RR      RR   EE              TT      RR      RR   AA      AA      TT
 CC          RR      RR   EE              TT      RR      RR   AA      AA      TT
 CC          RRRRRRRR     EEEEEEEE        TT      RRRRRRRR     AA      AA      TT
 CC          RRRRRRRR     EEEEEEEE        TT      RRRRRRRR     AA      AA      TT
 CC          RR  RR       EE              TT      RR  RR       AAAAAAAAAA      TT
 CC          RR  RR       EE              TT      RR  RR       AAAAAAAAAA      TT
 CC          RR    RR     EE              TT      RR    RR     AA      AA      TT
 CC          RR    RR     EE              TT      RR    RR     AA      AA      TT
   CCCCCCCC  RR      RR   EEEEEEEEEE      TT      RR      RR   AA      AA      TT
   CCCCCCCC  RR      RR   EEEEEEEEEE      TT      RR      RR   AA      AA      TT
```

```
FFFFFFFFFF    000000    RRRRRRRR        ;;;;        11        222222
FFFFFFFFFF    000000    RRRRRRRR        ;;;;        11        222222
FF          00      00  RR      RR      ;;;;      1111      22      22
FF          00      00  RR      RR      ;;;;      1111      22      22
FF          00      00  RR      RR                  11              22
FF          00      00  RR      RR                  11              22
FFFFFFFF    00      00  RRRRRRRR        ;;;;        11            22
FFFFFFFF    00      00  RRRRRRRR        ;;;;        11            22
FF          00      00  RR  RR          ;;;;        11          22
FF          00      00  RR  RR          ;;;;        11          22
FF          00      00  RR    RR          ;;        11        22
FF          00      00  RR    RR          ;;        11        22
FF            000000    RR      RR      ;;        111111    2222222222
FF            000000    RR      RR      ;;        111111    2222222222
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K    III    N   N
```

```
/VMS  PARKIN        CRETRAT  8-FEB-1984 08:01    LPAO:   8-FEB-1984 08:02    US:[DM.SI
/VMS  PARKIN        CRETRAT  8-FEB-1984 08:01    LPAO:   8-FEB-1984 08:02    US:[DM.SI
/VMS  PARKIN        CRETRAT  8-FEB-1984 08:01    LPAO:   8-FEB-1984 08:02    US:[DM.SI
```

```
C*************************************************************************************
C******                PROGRAM        CRETRAT.FOR
C******                ---------------------------------------
C******This program generates the transfer rate data block FILE11.DAT in FOR043
C******      Data is population by 100 single years of age, for each
C******     time period for which transfer rates required - in FOR042
C******        (Check format of FOR042...line 1100 9I4)
C******  Simple crude transfer rates in FICHE11.DAT read from FOR041
C*************************************************************************************
      INTEGER TIM1,TIM2,M,P,G,A
      DIMENSION IPOP(3,3,100)
      DIMENSION IRR(3,3)
      DIMENSION LINE(80)
      DIMENSION ITOTPOP(20)
      DIMENSION IPOPGP(3,3,20)
      DIMENSION WT(20)
      DIMENSION FACT(20)
      DIMENSION WR(20)
      DIMENSION FINR(3,3,20)
C~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
C     DATA BELOW ARE RELATIVE RISK(ALL AGES) OF 1-2 TRANSFER
C           BY M.S.(COLUMN) & PARITY(ROW)
C~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      DATA IRR/056,089,096,
     1          061,098,106,
     2          138,220,238/
      DATA ISLASH/1H//
C
C
 20   READ(42,1101,END=1000)LINE
       IF(LINE(1) .EQ. ISLASH)   GOTO  50
       BACKSPACE 42
      READ(42,1100)IPOP
      G=0
 50   READ(41,1101,END=1000)LINE
       IF(LINE(1) .EQ. ISLASH)   GOTO  900
       BACKSPACE 41
       READ(41,1102)IFR,ITO,IAG1,IAG2,TIM1,TIM2,RATE
        IF(IFR .NE. 1)     GOTO   400
        G=G+1
        ITOTPOP(G)=0
        DO 150 M = 1,3
          DO 145 P = 1,3
          IPOPGP(P,M,G)=0
            DO 140 A = IAG1,IAG2
 140         IPOPGP(P,M,G) = IPOPGP(P,M,G) + IPOP(P,M,A)
 145       ITOTPOP(G) = ITOTPOP(G) + IPOPGP(P,M,G)
 150    CONTINUE
C
C
        WT(G)=0.0
        DO 200 M = 1,3
          DO 200 P = 1,3
          WT(G) = WT(G) + (IPOPGP(P,M,G) * IRR(P,M)) / 100
 200    CONTINUE
        FACT(G) = ITOTPOP(G) / WT(G)
        WR(G) = RATE * FACT(G)
        DO 300 M = 1,3
          DO 300 P = 1,3
          FINR(P,M,G) = (WR(G) * IRR(P,M)) / 100
         WRITE(43,1103)IFR,ITO,IAG1,IAG2,P,M,TIM1,TIM2,FINR(P,M,G)
```

```
300     CONTINUE
        GO TO 50
400     M = 0
        P = 0
        WRITE(43,1103)IFR,ITO,IAG1,IAG2,P,M,TIM1,TIM2,RATE
        GO TO 50
900     WRITE(43,1101)ISLASH
        GO TO 20
1100    FORMAT(1X,9I4)
1101    FORMAT(80A1)
1102    FORMAT(1X,2(I2,1X),2(I3),2(I2,1X),F7.2)
1103    FORMAT(1X,2(I2,1X),2(I3),2(1X,I1),2(I2,1X),F10.6)
1000  STOP
      END
```

APPENDIX 4

THE SIMULATION PROGRAMME

```
C*****************************************************************************
C*****
C*****      S20 - THE MICRO-SIMULATION PROGRAM (VERSION XIV)
C*****        Accepts initial population size of 100,000
C*****
C*****        Input   : from 92 & 93 needed to provide duration of states
c*****                  2 and 3 in starting population (see  ST IST)
C*****        Outputs    1)  FOR008-new cancer deaths
C*****                   2)  FOR009-new cancer cases
C*****                   3)  FOR010-person-years at each age, each year
C*****                   4)  FOR034-tables, format of which must be specified
C*****                              in  FILE33.DAT
C*****      ORIGINAL BY P. HODGSON , MODIFIED BY DMP & MS
C*****
C*****************************************************************************
C*****************************************************************************
C*****
C           M A I N - L O G I C      S E C T I O N
C*****
C*****************************************************************************
C*****************************************************************************
C-----------------------------------------------------------------------------
C ADTNUM ........ TOTAL NUMBER OF THOSE AGED 15+(IE. IN 16TH OR MORE YEAR)
C ADULT(I) ...... CODED AGE, MS, IP, ISTAT, FOR THE I'TH ADULT
C INFANT(I) ..... NUMBER OF INFANTS AGED I
C INFNUM ........ TOTAL NUMBER OF THOSE IN THEIR 1ST TO 15TH YEARS
C INFTPC ........ NO PER 1000 DEEMED TO BE INFERTILE FROM BIRTH
C IYR ........... CURRENT SIMULATION YEAR
C NUMST ......... TOTAL NUMBER OF STATES INCLUDING +VES, DEAD STATES ETC
C NUMYRS ........ NUMBER OF YEARS IN SIMULATION
C POPSZE ........ TOTAL INITIAL POPLATION SIZE
C STHIS ......... STATE NUMBER OF 'DEAD OF THIS DISEASE'
C STHYST ........ STATE NUMBER OF 'HYSTERECTOMY STATE'
C STOTH ......... STATE NUMBER OF 'DEAD OF OTHER CAUSES'
C STPOS ......... STATE NUMBER OF 'POSTIVE SMEAR STATE'
C TIMES(I) ...... CODED ITIMM AND ICLOCK FOR I'TH ADULT
C-----------------------------------------------------------------------------
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
C-----------------------------------------------------------------------------
C        VARIABLES USED BY TRANSF SUBROUTINE:
C ITRATE(I) ... TRANSFER RATE OF I'TH LINE OF TRANSFER DATA
C ITRFR (I) ... FROM STATE FOR I'TH LINE
C ITRTO (I) ... TO STATE FOR I'TH LINE
C IAGMIN(I) ... MIN AGE FOR I'TH LINE
C IAGMAX(I) ... MAX AGE FOR I'TH LINE
C ITRMS (I) ... MARSTAT RATE IT APPLIES TO (0=ALL)
C ITRIP (I) ... PARA GROUP IT APPLIES TO (0=ALL)
C ITRTM1(I) ... TIME IN STATE FROM VALUE IT APPLIES TO
C ITRTM2(I) ... TIME IN STATE TO VALUE IT APLLIES TO
C IOST ........ ORIGINAL STATE - BEFORE ANY TRANSFERS BEGIN
C ISCPOSBK(I,J). RATE OF REVERSION TO ORIGINAL STAYE(I) FROM STPOS
C NUMTR ....... NUMBER OF LINES OF TRANSFER DATA
C-----------------------------------------------------------------------------
      COMMON /TRSVAR/ ITRATE(500), ITRFR (500), ITRTO (500),
     1                IAGMIN(500), IAGMAX(500),
     2                ITRMS (500), ITRIP (500), ITRTM1(500), ITRTM2(500)
C-----------------------------------------------------------------------------
```

```
C         VARIABLES USED BY SCREEN SUBROUTINE:
C ISCYR (I,J) .  (I,1) IS START YR, (I,2) END YR OF I'TH POLICY
C ISCINT  (I) .  SCREENING INTERVAL FOR I'TH SCREEN POLICY
C ISCAGE(I,J) .  (I,1) IS START AGE, (I,2) END AGE FOR I'TH POL
C ISCMS   (I) .  MARSTAT OF I'TH POLICY TARGET POP'N (0=ALL)
C ISCIP   (I) .  PARITY  OF I'TH POLICY TARGET POP'N (0=ALL)
C ISCATT(I,J) .  ATT RATE (%) OF J'TH STATE IN I'TH POLICY
C ISCPOS(I,J) .  POS RATE (%) OF J'TH STATE IN I'TH POLICY
C ISCPOSBK(I,J). RATE OF REVERSION TO ORIGINAL STATE(I) FROM STPOS
C ISCTOT..... NUMBER OF SCREENING TESTS IN YEAR
C ISCNA..... NUMBER OF ELLIGIBLE NON-ATTENDERS IN YEAR
C ISCGTOT..... NUMBER OF SCREENING TESTS SINCE YEAR 0
C ISCGNA..... NUMBER OF ELLIGIBLE NON-ATTENDERS SINCE YEAR 0
C IPOSTGT(I)... NUMBER OF POS. TESTS SINCE TIME 0 IN STATE I
C NUMSCR ..... NUMBER OF POLICIES IN SCREENING CAMPAIGN
C-----------------------------------------------------------------------
      COMMON /SCRVAR/ ISCYR(20,2),ISCINT(20)  ,ISCAGE(20,2)  ,ISCMS(20),
     1   ISCIP(20) ,ISCATT(20,6),ISCPOS(20,6),ISCPOSBK(20,6),IPOSTGT(6),
     2   ISCTOT,ISCNA,ISCGTOT,ISCGNA
C-----------------------------------------------------------------------
C         VARIABLES USED BY AGEING SUBROUTINE:
C ICHILD(I,J,K) ... CHANCE IN 1000 THAT A WOMAN AGED I, MS J, IP K HAS A KID
C IHYST (I) ..... CHANCE OF HAVING HYSTERECTOMY AT AGE I
C IMARRY(I,J,K) ... CHANCE OF MOVING TO MS K GIVEN AGE I AND MS J
C IPOPT (I) ..... TOTAL NUMBER OF WOMEN AGED I
C ISTOT (I) ..... TOTAL NUMBER OF WOMEN IN STATE I
C ITRMAT(I,J) ..... NUMBER TRANSFERRING FROM STATE I TO STATE J IN YEAR
C MORT  (I) ..... CHANCE OF DYING IF AGED I
C XPFACT(I,J)..... CORRECTION FACTOR FOR ICHILD(I,J,1)
C-----------------------------------------------------------------------
      COMMON /AGEVAR/ ICHILD(100,3,3),IHYST(100),
     1                IMARRY(100,3,3),MORT (100),
     1                XPFACT(100,3)
C-----------------------------------------------------------------------
      COMMON /SUMVAR/ ISTOT(10),ITRMAT(10,10)
C-----------------------------------------------------------------------
C         VARIABLES ADDED  FOR TABULATION PURPOSE
C NXYRTPRT ..... NEXT YEAR FOR WHICH OUTPUT IS REQUIRED
C TABCOUNTS ..... INTEGER ARRAY TO HOLD COUNTS
C LWBNDS ..... LOWER BOUNDS FOR DIMENSIONS
C UPBNDS ..... UPPER BOUNDS FOR DIMENSIONS
C NTABDIMS ..... NUMBER OF DIMENSIONS IN TABULATION
C VARNUM ..... NUMMER OF VARIABLES USED FOR TABULATION
C                  1. AGE
C                  2. MS
C                  3. PARITY
C                  4. STATUS
C                  5. TIME IN STATE
C                  6. CLOCK YEARS
C                  7. PREV STATE
C NVARCL ..... NUMBER OF CLASSES FOR VARIABLES
C INDVAL ..... THE 7 VALUES FOR AN INDIVIDUAL
C LWCLVAL ..... LOWER VALUE FOR ONE CLASS
C UPCLVAL ..... UPPER VALUE FOR ONE CLASS
C-----------------------------------------------------------------------
      INTEGER NXYRTPRT,TABCOUNTS(20000),LWBNDS(10),UPBNDS(10)
      INTEGER NTABDIMS,VARNUM(10),NVARCL(10),INDVAL(7)
      INTEGER LWCLVAL(10,100),UPCLVAL(10,100)
C-----------------------------------------------------------------------
C         INITIAL SUBROUTINES:
C INIT ----- READS IN INITIAL DATA & PRINTS MAIN HEADINGS
```

```
C ST AGE --- GENERATES STARTING AGES
C ST MST --- GETS STARTING MARSTAT FROM AGE
C ST IPS --- GETS STARTING PARA FROM AGE & MARSTAT
C ST IST --- GETS STARTING STATE FROM PARA, MARSTAT & AGE
C-----------------------------------------------------------------------
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C THE FOLLOWING SUBROUTINES ARE CALLED ONCE ONLY AT BEGINNING OF SIMULATION
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      CALL INIT   (IPRTYR)
      CALL ST AGE
      CALL ST MST
      CALL ST IPS (INFTPC)
      CALL ST IST (IPRTYR)
C
        IYR=0
C
10      READ (33,*,END=11) NXYRTPRT
        READ (33,*) NTABDIMS
        DO IDIM=1,NTABDIMS
           READ (33,*) VARNUM(IDIM),NVARCL(IDIM)
           LWBNDS(IDIM)=1
           UPBNDS(IDIM)=NVARCL(IDIM)
           DO IVCL=1,NVARCL(IDIM)
              READ (33,*) LWCLVAL(IDIM,IVCL),UPCLVAL(IDIM,IVCL)
           END DO
        END DO
        GOTO 20
C
11      NXYRTPRT=999999
C
20      IF ( IYR.GT.NXYRTPRT ) GOTO 10
        IF ( IYR.LT.NXYRTPRT ) GOTO 100
C
C       DO THE TABULATION
        CALL TABINI(TABCOUNTS,NTABDIMS,LWBNDS,UPBNDS)
        DO IREC=1,ADTNUM
           CALL DECODE(IREC,INDVAL(1),INDVAL(2),INDVAL(3),INDVAL(4))
           CALL DECTIM(IREC,INDVAL(5),INDVAL(6),INDVAL(7))
           DO IDIM=1,NTABDIMS
              IVN=VARNUM(IDIM)
              IVAL=INDVAL(IVN)
              DO IVCL=1,NVARCL(IDIM)
                 IF ( IVAL.GE.LWCLVAL(IDIM,IVCL) .AND.
     1                IVAL.LE.UPCLVAL(IDIM,IVCL) ) GOTO 30
              END DO
C             AT THAT POINT INDIVIDUAL IREC IS UNCLASSIFIABLE
C             JUST FORGET IT
              GOTO 50
30            LWBNDS(IDIM)=IVCL
           END DO
           CALL TABADD(1,TABCOUNTS,LWBNDS)
50         CONTINUE
        END DO
C
C       NOW COUNT THOSE AGE 15 OR LESS
C
        INDVAL(2)=1
        INDVAL(3)=0
        INDVAL(4)=1
        INDVAL(6)=0
        INDVAL(7)=1
```

```
          DO I=1,15
             INDVAL(1)=I
             INDVAL(5)=I
             DO IDIM=1,NTABDIMS
                IVN=VARNUM(IDIM)
                IVAL=INDVAL(IVN)
                DO IVCL=1,NVARCL(IDIM)
                   IF ( IVAL.GE.LWCLVAL(IDIM,IVCL) .AND.
          1             IVAL.LE.UPCLVAL(IDIM,IVCL) ) GOTO 31
                END DO
C               AT THAT POINT INDIVIDUAL IREC IS UNCLASSIFIABLE
C               JUST FORGET IT
                GOTO 51
31              LWBNDS(IDIM)=IVCL
             END DO
             CALL TABADD(INFANT(I),TABCOUNTS,LWBNDS)
51           CONTINUE
          END DO
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C         OUTPUT RESULT OF TABULATION TO NEWFILE FOR034
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
          OPEN ( UNIT=34, STATUS='NEW' )
          CALL TABOUT(TABCOUNTS,34)
          CLOSE (34)
C
          GOTO 10
C
100       IYR=IYR+1
          IF ( IYR.GT.NUMYRS ) STOP
C-------------------------------------------------------------------------------
C          YEAR ON YEAR SUBROUTINES:
C TRANSF --- PERFORMS THE TRANSFERS BETWEEN STATES
C SCREEN --- DOES ANY SCREENING CALLED FOR THAT YEAR
C AGEING --- PRINTS YR SUMMARY, AGES THEM AND ADDS NEW ONES TO END OF LIST
C-------------------------------------------------------------------------------
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C THE FOLLOWING SUBROUTINES ARE CALLED DURING EACH SIMULATION YEAR
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C
            CALL TRANSF
C
            CALL SCREEN
C
            CALL AGEING (INFTPC,IPRTYR)
C
          GOTO 20
C
          END
C-------------------------------------------------------------------------------
C          OTHER SUBROUTINES:
C RAND(I,J) ............. PRODUCES RANDOM INTEGER, I, IN RANGE 1-J
C ENCODE(I,list)......... ENCODES I'TH PERSON'S list OF AGE,MS,IP ETC
C ENCTIM(I,ITME,ICL,LST). ENCODES I'TH TIME IN STATE, CLOCK YEARS & PREV STATE
C DECODE(I,list)......... DECODES I'TH PERSON'S list OF AGE,MS,IP ETC
C DECTIM(I,ITME,ICL,LST). DECODES I'TH TIME IN STATE, CLOCK YEARS & PREV STATE
C TABLES................. PRINTS OUTPUT TABLES TO CHANNEL 8
C-------------------------------------------------------------------------------
C
```

```
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E     I N I T
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE,STHYST,STPOS,STHIS,STOTH,ADTNUM
      INTEGER ADULT,TIMES,DEAD
      COMMON POPSZE,NUMST,NUMYRS,STHYST,STPOS,STHIS,STOTH,INFNUM
      COMMON ADTNUM,IYR
      COMMON INFANT(15),ADULT(109999),TIMES(109999),DEAD(100)
      COMMON /SCRVAR/ ISCYR(20,2),ISCINT(20)  ,ISCAGE(20,2)  ,ISCMS(20),
     1   ISCIP(20) ,ISCATT(20,6),ISCPOS(20,6),ISCPOSBK(20,6),IPOSTGT(6),
     2   ISCTOT,ISCNA,ISCGTOT,ISCGNA
C-------------------------------------------------------------------------------
C ISCTOT ..... TOTAL NUMBER OF PEOPLE SCREENED IN CURRENT YEAR
C-------------------------------------------------------------------------------
      WRITE(6,600)
       DO 10 I = 1,6
       IPOSTGT(I) = 0
  10   CONTINUE
      ISCTOT = 0
      ISCNA  = 0
      ISCGTOT = 0
      ISCGNA = 0
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C READ IN AND VALIDATE POP'N SIZE, NUMBER OF STATES AND YEARS IN SIMULATION
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      READ(1,1101) POPSZE,NUMST
      IF(POPSZE.GT.50.AND.POPSZE.LE.100001) GOTO 20
      WRITE(6,601) POPSZE
      STOP
   20 IF(NUMST.GT.4 .AND.NUMST .LE.10  ) GOTO 30
      WRITE(6,602) NUMST
      STOP
   30 STOTH = NUMST
      STHIS = NUMST-1
      STHYST= NUMST-2
      STPOS = NUMST-3
      READ(1,1101,END=40) NUMYRS
      IF(NUMYRS.GT.0.AND.NUMYRS.LT.31) GOTO 50
   40 WRITE(6,603)
      STOP
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C DUMMY READ(YEARS FOR OUTPUT FILE NOT USED IN THIS VERSION)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
   50 READ(1,1102)
      RETURN
   80 WRITE(6,604)
      STOP
  600 FORMAT(//20X,'THE I.A.R.C. CERVICAL CYTOLOGY SCREENING MODEL'
     1         /20X,'_____'
     2     ////)
  601 FORMAT(' ** ERR IN FILE1 -- POPSZE',I3,' INCORRECT **')
  602 FORMAT(' ** ERR IN FILE1 -- NUMBER',I3,' OF STATES **')
  603 FORMAT(' ** ERR IN FILE1 -- NUMYRS INCORRECT **')
  604 FORMAT(' ** ERR IN FILE1 -- FOR008 YRS **')
 1101 FORMAT(I8)
 1102 FORMAT(1X)
      END
```

```
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E     S T   A G E
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
      COMMON /SUMVAR/ ISTOT(10), ITRMAT(10,10)
C-------------------------------------------------------------------------------
C ICUMUL(I) ..... NUMBER OF PEOPLE IN TARGET POP'N WITH AGE LE I
C IPOP  (I) ..... NUMBER OF PEOPLE IN TARGET POP'N WITH AGE EQ I
C ITOT .......... TOTAL NUMBER OF PEOPLE IN TARGET POP'N
C-------------------------------------------------------------------------------
      DIMENSION ICUMUL(100), IPOP(100)
      READ(1,1105) IPOP
      ITOT=0
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CALCULATE THE AGE CUMULATIVE POPULATION TOTALS AS WELL AS TOTAL POPULATION
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 50 I=1,100
          ICUMUL(I) = 0
          ICUMUL(I) = ITOT + IPOP(I)
          ITOT      = ICUMUL(I)
   50     CONTINUE
      INFNUM=0
      ADTNUM=0
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C FOR EACH OF THE REQUESTED INITIAL POP'N GENERATE THEIR AGE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 100 I=1,POPSZE
          CALL RAND(J,ITOT)
          DO 70 K=1,100
              IF(J.LE.ICUMUL(K)) GOTO 80
   70         CONTINUE
          WRITE(6,601)
          STOP
   80     IF(K.EQ.100) K=100
          IF(K.GT.15)  GOTO 90
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C FOR AN INFANT SIMPLY INCREMENT THE CORRECT VALUE IN ARRAY INFANT
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
          INFNUM   =INFNUM   +1
          INFANT(K)=INFANT(K)+1
          GOTO 100
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C FOR AN ADULT, CALL ENCODE TO STORE THEIR AGE IN THE ADULT ARRAY
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
   90     ADTNUM=ADTNUM+1
          CALL ENCODE(ADTNUM,K,1,1,1)
  100     CONTINUE
 1101 FORMAT(I8/I8).
 1105 FORMAT(10I8)
  601 FORMAT(' ** ERR IN PROG, SR ST.AGE **')
      RETURN
      END
C
```

```
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E     S T   M S T
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
C-------------------------------------------------------------------------------
C IMAR(I,J) ..... NUMBER OF PEOPLE (PER 1000) IN TARGET POP'N
C                 AGED I WHO HAVE MARSTAT J
C-------------------------------------------------------------------------------
      DIMENSION IMAR(100,3)
      READ (2,1201) ((IMAR(I,J),J=1,3),I=1,100)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CONVERT THE INPUT PROBABILITY DISTRIBUTION INTO CUMULATIVE PROBABILITIES
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 50 I=1,100
          IMAR(I,2) = IMAR(I,2) + IMAR(I,1)
          IMAR(I,3) = IMAR(I,3) + IMAR(I,2)
          IF(IMAR(I,3).EQ.1000) GOTO 50
          WRITE(6,601) I
          STOP
   50     CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C FOR EACH ADULT GENERATE STARTING MARSTAT WITH REGARD TO AGE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 100 I=1,ADTNUM
          CALL DECODE(I,IAG,MS,IP,IST)
          CALL RAND(J,1000)
          DO 70 K=1,3
              IF(J.LE.IMAR(IAG,K)) GOTO 80
   70         CONTINUE
          WRITE(6,602)
          STOP
   80     CALL ENCODE(I,IAG,K,1,1)
  100     CONTINUE
      RETURN
  601 FORMAT(' ** ERR IN LINE',I4,' IN INIT MAR DIST')
  602 FORMAT(' ** PROG ERR IN SR ST MST')
 1201 FORMAT(1X,3I4)
      END
C
```

```
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E     S T   I P S (INFTPC)
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
      COMMON /AGEVAR/ ICHILD(100,3,3), IHYST(100),
     1                IMARRY(100,3,3), MORT (100),
     1                XPFACT(100,3)
C-------------------------------------------------------------------------------
C IPAR(I,J,K) ..... NUMBER OF PEOPLE (PER 1000) IN TARGET POP'N AGED I AND
C                   MARSTAT J WHO HAVE PARA K
C-------------------------------------------------------------------------------
      DIMENSION IPAR(100,3,3)
      DIMENSION XIPAR(100,3,1)
      READ(3,1301) INFTPC
      READ(3,1301) (((IPAR(I,J,K),K=1,3),J=1,3),I=1,100)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CALCULATE FACTOR(XPFACT) THAT WILL BE USED IN AGEING SUBROUTINE TO CORRECT
C THE PROBABILITIES OF HAVING A FIRST CHILD, GIVEN INFERTILITY IN SOME WOMEN
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
       XINFTPC = FLOAT(INFTPC)
       DO 10 I=1,100
         DO 10 J=1,3
           XIPAR(I,J,1)=FLOAT(IPAR(I,J,1))
           IF( XINFTPC.LT.XIPAR(I,J,1) ) GOTO 5
           WRITE(6,600)
           STOP
   5       XPFACT(I,J) = 1.0 - (XINFTPC / XIPAR(I,J,1))
  10   CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CORRECT THE PARITY PROPORTIONS TO ALLOW FOR INFERTILE WOMEN (PARA 0) &
C CONVERT THE INPUT PROBABILITY DISTRIBUTION INTO CUMULATIVE PROBABILITIES
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 50 I=1,100
         DO 40 J=1,3
           IPAR(I,J,3) = IFIX (FLOAT(IPAR(I,J,3))/((1000-INFTPC)/1000.))
           IPAR(I,J,2) = IFIX (FLOAT(IPAR(I,J,2))/((1000-INFTPC)/1000.))
           IPAR(I,J,1) =  1000 - IPAR(I,J,2) - IPAR(I,J,3)
              IPAR(I,J,2) = IPAR(I,J,2) + IPAR(I,J,1)
              IPAR(I,J,3) = IPAR(I,J,3) + IPAR(I,J,2)
              IF(IPAR(I,J,3).EQ.1000) GOTO 40
              WRITE(6,601) I
              STOP
   40         CONTINUE
   50    CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C FOR EACH ADULT GENERATE PARA ACCORDING TO AGE AND MARITAL STATUS
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 100 I=1,ADTNUM
         CALL DECODE(I,IAG,MS,IP,IST)
   60    CALL RAND(J,1000)
```

```
      DO 70 IP=1,3
          IF(J.LE.IPAR(IAG,MS,IP)) GOTO 80
   70     CONTINUE
      WRITE(6,602)
      STOP
   80 CALL RAND(J,1000)
      IF(J.GT.INFTPC) GOTO 90
      IP=0
   90 CALL ENCODE(I,IAG,MS,IP,IST)
  100 CONTINUE
      RETURN
  600 FORMAT(' PROPORTION INFERTILE IN DATA FILE3 IMPOSSIBLY LARGE')
  601 FORMAT(' ** ERR IN LINE',I4,' OF INIT PAR DIST')
  602 FORMAT(' ** ERR IN PROG IN ST IPS SR')
 1301 FORMAT(3X,9I4)
      END
C
```

```
C*************************************************************************
C*************************************************************************
C*****
      S U B R O U T I N E     S T   I S T
C*****
C*************************************************************************
C*************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
C-------------------------------------------------------------------------
C DIST ..........  NUMBER OF 'ORDINARY' DISEASE STATES (USUALLY 4?)
C HYST(I) ........ NUMBER (PER 100,000) OF TARGET POP'N AGED I WITH HYSTERECTY
C ISTOT(I) ....... TOTAL NUMBER IN STATE I AT BEGINNING OF SIMULATION
C STCUM(I,J,K,L) . CUMUL. PROB OF BEING AGED I, MS J, IP K AND IN STATE L
C IADMAT2(I,J).... CUMULATIVE PROBABILITY OF DURATION(J) IN ST 2 AT AGE I
C IADMAT3(I,J).... CUMULATIVE PROBABILITY OF DURATION(J) IN ST 3 AT AGE I
C-------------------------------------------------------------------------
      INTEGER STCUM, HYST
      DIMENSION HYST(100), STCUM(100,3,3,8), ISTOT(10)
      DIMENSION IADMAT2(70,75), IADMAT3(70,75)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C READ IN STARTING PROBABILITY OF HAVING HYSTERECTOMY AT EACH AGE YEAR
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      READ(1,1101) HYST
      DIST = STPOS-1
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C READ IN PROB. DIST. OF OTHER STATES AND, WITH HYST DATA, MAKE CUM. PROBS
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 40 I=1,100
          DO 30 J=1,3
              DO 20 K=1,3
                  READ(4,1401) (STCUM(I,J,K,L),L=1,DIST)
                  STCUM(I,J,K,STHYST)=HYST(I)
                  STCUM(I,J,K,1      )=STCUM(I,J,K,1)-HYST(I)
                  STCUM(I,J,K,STPOS )=0
                  DO 10 L=2,STHYST
                      STCUM(I,J,K,L)=STCUM(I,J,K,L   )
     1                               +STCUM(I,J,K,L-1)
   10                 CONTINUE
                  IF(STCUM(I,J,K,STHYST).EQ.10000) GOTO 20
                  WRITE(6,601)STCUM(I,J,K,1),I,J,K
                  STOP
   20             CONTINUE
   30         CONTINUE
   40     CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C READ IN AGE/DURATION MATRICES FOR STATES 2 , 3   FROM CHANNELS 92 , 93
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
          DO 50 I = 1,70
          READ(92,901)(IADMAT2(I,J),J=1,75)
          READ(93,901)(IADMAT3(I,J),J=1,75)
   50     CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C GENERATE STARTING STATE FOR EACH ADULT WITH REGARD TO AGE, MARSTAT AND PARA
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 100 I=1,ADTNUM
          CALL DECODE(I,IAG,MS,IP,IST)
          IPT = IP
```

```
          IF(IPT.EQ.0) IPT = 1
          CALL RAND(J,10000)
          DO 70 K=1,STHYST
              IF(J.LE.STCUM(IAG,MS,IPT,K)) GOTO 80
   70         CONTINUE
          WRITE(6,602)
          STOP
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C              IF STATE=1 THEN TIME IN STATE IS AGE
C   OTHERWISE READ FROM CHANNELS 92,93.... AS IADMATx(age,dur) MATRIX
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
   80     IF(K.NE.1) GOTO 82
          ITIMM = IAG
          GOTO 95
   82     IF(K.NE.2) GOTO 84
           CALL RAND(L,100)
           M = IAG - 15
           IF(M.GT.70) M=70
            DO 83 N = 1,75
            ITIMM = N
            IF(L.LE.IADMAT2(M,N)) GO TO 95
   83       CONTINUE
          GOTO 95
   84     IF(K.NE.3) GOTO 86
           CALL RAND(L,100)
           M = IAG - 15
           IF(M.GT.70) M=70
            DO 85 N = 1,75
            ITIMM = N
            IF(L.LE.IADMAT3(M,N)) GO TO 95
   85       CONTINUE
          GOTO 95
   86     IF(K.NE.4) GOTO 88
          CALL RAND(L,100)
          ITIMM = L/50 + 1
          GOTO 95
   88     IF(K.NE.5) GOTO 90
          CALL RAND(L,100)
          ITIMM =  1
          IF(L.LT.70)ITIMM=2
          IF(L.LT.65)ITIMM=3
          IF(L.LT.50)ITIMM=4
          IF(L.LT.40)ITIMM=5
          GOTO 95
   90     ITIMM = 1
   95     CALL ENCODE(I,IAG,MS,IP,K)
          CALL ENCTIM(I,ITIMM,ICLOCK,K)
  100     CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C PRINT THE STARTING POPULATION'S DISTRIBUTION AMONGST STATES AND POPN SIZE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  140 DO 150 I=1,NUMST
          ISTOT(I) = 0
  150     CONTINUE
      DO 160 I=1,15
          ISTOT(1) = ISTOT(1) + INFANT(I)
  160     CONTINUE
      DO 180 I=1,ADTNUM
          CALL DECODE(I,IAG,MS,IP,IST)
          ISTOT(IST) = ISTOT(IST) + 1
  180     CONTINUE
```

```
      ITTOT = 0
      WRITE(6,603)
      DO 200 I=1,NUMST
          ITTOT = ITTOT + ISTOT(I)
          WRITE(6,604) I,ISTOT(I)
  200     CONTINUE
      WRITE(6,605) ITTOT
      RETURN
  601 FORMAT(' ** ERR IN STATE DATA ..AGE,MS,IP.. ',3I4)
  602 FORMAT(' ** ERR IN PROG IN ST IST SR')
  603 FORMAT(20X,'Y E A R  0'/20X,'----------')
  604 FORMAT(' NUMBER IN STATE ',I2,' ...  ',I8)
  605 FORMAT(/' TOTAL POPULATION .....  ',I8///)
  801 FORMAT(8I3)
  901 FORMAT(4X,25I3,/,4X,25I3,/,4X,25I3)
 1101 FORMAT(10I8)
 1401 FORMAT(1X,6I5)
      END
C
```

```
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E    T R A N S F
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE,STHYST,STPOS,STHIS,STOTH,ADTNUM
      INTEGER ADULT,TIMES,DEAD
      COMMON POPSZE,NUMST,NUMYRS,STHYST,STPOS,STHIS,STOTH,INFNUM
      COMMON ADTNUM,IYR
      COMMON INFANT(15),ADULT(109999),TIMES(109999),DEAD(100)
      COMMON /SUMVAR/ ISTOT(10),ITRMAT(10,10)
      COMMON /TRSVAR/ ITRATE(500),ITRFR (500),ITRTO (500),
     1                IAGMIN(500),IAGMAX(500),
     2                ITRMS (500),ITRIP (500),ITRTM1(500),ITRTM2(500)
      COMMON /SCRVAR/ ISCYR(20,2),ISCINT(20)  ,ISCAGE(20,2)  ,ISCMS(20),
     1   ISCIP(20) ,ISCATT(20,6),ISCPOS(20,6),ISCPOSBK(20,6),IPOSTGT(6),
     2   ISCTOT,ISCNA,ISCGTOT,ISCGNA
      INTEGER TIM1,TIM2
      DIMENSION LINE   (80)
C-------------------------------------------------------------------------------
C IAG1-IAG2.  FROM AGE TO AGE (AS YEAR OF LIFE) READ IN FROM FILE
C IFR .....  FROM STATE READ IN FROM FILE
C ISLASH ...  '//' MARKS END OF TRANSFER RATE DATA
C ITO .....  TO STATE READ IN FROM FILE
C LINE .....  INPUT LINE ARRAY USED TO SEARCH FOR '//' WHICH MARKS END OF FILE
C NUMTR ....  NUMBER OF LINES OF TRANSFER RATE DATA
C RATE .....  TRANSFER RATE READ IN FROM FILE
C TIM1 .....  FROM 'TIME IN STATE' READ IN FROM FILE
C TIM2 .....  TO   'TIME IN STATE' READ IN FROM FILE
C ISCPOSBK..  PERCENT REVERTING TO ORIGINAL STATE FROM STPOS
C             (ONLY POSSIBLE AFTER YEAR 1)
C-------------------------------------------------------------------------------
      DATA ISLASH/1H//
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF YEAR IS 1 OR 11 OR 21 THEN READ IN A TRANSFER RATE DECLARATION FILE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IF(IYR.NE.1.AND.IYR.NE.11.AND.IYR.NE.21) GOTO 100
      NUMTR=1
   50 READ(11,1101,END=90) LINE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF THE INPUT LINE WAS NOT '//' THEN READ IT AGAIN AS A LINE OF TRANSFER DATA
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IF(LINE(1).EQ.ISLASH) GOTO 90
      BACKSPACE 11
      READ(11,1102) IFR,ITO,IAG1,IAG2,MS,IP,TIM1,TIM2,RATE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF ANY OF ITEMS IN TRANSFER FILE IS OUT OF RANGE THEN PRINT MESSAGE AND STOP
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IF(IFR .LT. 1.OR.IFR .GT.STPOS) GOTO 80
      IF(ITO .LT. 1.OR.ITO .GT.STHIS) GOTO 80
      IF(IAG1.LT.16.OR.IAG1.GT.100   ) GOTO 80
      IF(IAG2.LT.16.OR.IAG2.GT.100   ) GOTO 80
      IF(MS  .LT. 0.OR.MS  .GT.3     ) GOTO 80
      IF(IP  .LT. 0.OR.IP  .GT.3     ) GOTO 80
      IF(TIM1.LT. 0.OR.TIM1.GT.100   ) GOTO 80
      IF(TIM2.LT. 1.OR.TIM2.GT.100   ) GOTO 80
      IF(RATE.LT. 0.OR.RATE.GT.100.0) GOTO 80
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C PUT VALIDATED ITEMS INTO TRANSFER ARRAYS AND INCREMENT NUMBER OF LINES USED
```

```
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      ITRATE(NUMTR)  = IFIX(RATE * 1 000 000.0)
      ITRFR (NUMTR)  = IFR
      ITRTO (NUMTR)  = ITO
      IAGMIN(NUMTR)  = IAG1
      IAGMAX(NUMTR)  = IAG2
      ITRMS (NUMTR)  = MS
      ITRIP (NUMTR)  = IP
      ITRTM1(NUMTR)  = TIM1
      ITRTM2(NUMTR)  = TIM2
      NUMTR = NUMTR+1
      GOTO 50
   80 WRITE(6,601) NUMTR
      STOP
   90 NUMTR = NUMTR-1
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C SET ALL ELEMENTS OF STATE TRANSITION MATRIX THAT WILL BE USED TO ZERO
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  100  DO 120 I=1,NUMST
          DO 110 J=1,NUMST
              ITRMAT(I,J)=0
  110         CONTINUE
  120     CONTINUE
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C INCREMENT MATRIX FOR INFANTS WHO MUST DO A STATE 1 TO STATE 1 TRANSITION
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 130 I=1,15
          ITRMAT(1,1) = ITRMAT(1,1) + INFANT(I)
  130     CONTINUE
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C INCREMENT MATRIX FOR ADULTS ON BASIS OF THEIR STATE AT START OF YEAR
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 500 I=1,ADTNUM
          CALL DECODE(I,IAG,MS,IP,IST)
          CALL DECTIM(I,ITIMM,ICLOCK,LSTAT)
          IPT = IP
          IF(IPT.EQ.0) IPT = 1
          ITRMAT(IST,IST) = ITRMAT(IST,IST) + 1
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C FIRST,FOR ALL EXCEPT YEAR 1,(AT THE BEGINNING OF WHICH NO ONE IS IN STPOS)
C RETURN WOMEN IN STPOS TO THEIR ORIGINAL PRESCREEN STATE
C ACCORDING TO RATES SPECIFIED IN LINE 3 OF FILE 12
C (N.B.  OPERATES FOR FIRST 3 YEARS AFTER DETECTION ONLY)
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  140  IOST = IST
       IF(IYR  .EQ.  1)     GO TO 155
       IF(IST  .NE.  STPOS) GO TO 155
       IF(ITIMM.GT.  3)     GO TO 155
       CALL RAND(K,100)
       IF(K .GT. ISCPOSBK(1,LSTAT)) GO TO 155
       IST = LSTAT
       LSTAT=STPOS
       ITIMM=0
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C THE MAIN LOOP FOR EXAMINING WOMEN FOR TRANSFERS BETWEEN STATES BEGINS HERE
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  155     IFACT = 1
  160     DO 200 J=1,NUMTR
              IF (IST    .NE. ITRFR (J))                    GOTO 200
              IF (IAG    .LT. IAGMIN(J))                    GOTO 200
              IF (IAG    .GT. IAGMAX(J))                    GOTO 200
```

```
              IF (MS      .NE. ITRMS (J) .AND. ITRMS(J) .NE. 0) GOTO 200
              IF (IPT     .NE. ITRIP (J) .AND. ITRIP(J) .NE. 0) GOTO 200
              IF (ITIMM   .LT. ITRTM1(J))                       GOTO 200
              IF (ITIMM   .GT. ITRTM2(J))                       GOTO 200
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF THIS TRANSFER IS A POSSIBLE ONE THEN GET RANDOM NUMBER TO SEE IF IT OCCURS
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
              CALL RAND(K, 100 000 000)
              IF (K*IFACT.GT.ITRATE(J))                         GOTO 200
              IST = ITRTO(J)
              LSTAT = ITRFR(J)
              ITIMM = 0
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C AFTER A TRANSFER HAS OCCURED, GO BACK FOR ANOTHER (BUT WITH REDUCED PROB)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
              IFACT = IFACT * 2
              GOTO 160
  200         CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C INCREMENT THE TRANSITION MATRIX IF CHANGE OF STATE HAS TAKEN PLACE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  300      IF(ITIMM .NE. 0 .OR. IST .EQ. IOST)  GO TO 400
           ITRMAT(IOST, IST  ) = ITRMAT(IOST, IST  ) + 1
           ITRMAT(IOST, IOST) = ITRMAT(IOST, IOST) - 1
  400          CALL ENCODE(I, IAG, MS, IP, IST)
               CALL ENCTIM(I, ITIMM, ICLOCK, LSTAT)
  500      CONTINUE
       RETURN
  601  FORMAT(' ** ERR IN LINE', I4, ' OF TRANSF RATE DATA')
 1101  FORMAT(80A1)
 1102  FORMAT(1X, 2(I2, 1X), 2(I3), 2(1X, I1), 2(I2, 1X), F10.6)
       END
C
```

```
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E    S C R E E N
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
      COMMON /SUMVAR/ ISTOT(10), ITRMAT(10, 10)
      COMMON /SCRVAR/ ISCYR(20, 2), ISCINT(20)  , ISCAGE(20, 2)  , ISCMS(20),
     1   ISCIP(20) , ISCATT(20, 6), ISCPOS(20, 6), ISCPOSBK(20, 6), IPOSTGT(6),
     2   ISCTOT, ISCNA, ISCGTOT, ISCGNA
      DIMENSION LINE (80)
C-------------------------------------------------------------------------------
C DIST ..................  NUMBER OF DISEASE STATES BEFORE '+VE SMEAR'
C IATT(I) ...............  TEMP ARRAY FOR I'TH POLICY ATT DATA
C IPOS(I) ...............  TEMP ARRAY FOR I'TH POLICY +VE DATA
C IPOSBK(I)..............  TEMP ARRAY FOR PCT REVERTING TO ORIG STATE
C ISLASH ................  '//' MARKS END OF SCREENING DATA FILE
C LINE ..................  INPUT LINE ARRAY USED TO SEARCH FOR '//'
C NUMSCR ................  NUMBER OF POLICIES IN TOTAL SCREENING POLICY
C-------------------------------------------------------------------------------
      DIMENSION IATT(6), IPOS(6), IPOSBK(6)
      DATA ISLASH /1H//
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C FILE CONTAINING INFORMATION ABOUT SCREENING CAMPAIGN IS ONLY READ IN YEAR 1
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IF(IYR.NE.1) GOTO 100
      DIST =STPOS-1
      NUMSCR=1
   50 READ(12, 1201, END=90) LINE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF INPUT LINE WAS NOT END OF FILE THEN READ THREE LINES OF SCREENING DATA
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IF(LINE(1).EQ.ISLASH) GOTO 90
      BACKSPACE 12
      READ(12, 1202, END=80) IYR1, IYR2, INT, IAG1, IAG2, MS, IP, IATT
      READ(12, 1203, END=80) IPOS
      READ(12, 1203, END=80) IPOSBK
      IF(IYR1.LT.1961.OR.IYR1.GT.1990) GOTO 80
      IF(IYR2.LT.1961.OR.IYR2.GT.1990) GOTO 80
      IF(INT .LT.1    .OR.INT .GT.25   ) GOTO 80
      IF(IAG1.LT.16   .OR.IAG1.GT.100  ) GOTO 80
      IF(IAG2.LT.16   .OR.IAG2.GT.100  ) GOTO 80
      IF(MS  .LT.0    .OR.MS  .GT.3    ) GOTO 80
      IF(IP  .LT.0    .OR.IP  .GT.3    ) GOTO 80
      DO 60 I=1, DIST
          IF(IATT(I).LT.0.OR.IATT(I).GT.100) GOTO 80
          ISCATT (NUMSCR, I) = IATT(I)
          IF(IPOS(I).LT.0.OR.IPOS(I).GT.999) GOTO 80
          IF(IPOS(I).EQ.999) IPOS(I)=1000
          ISCPOS (NUMSCR, I) = IPOS(I)
          IF(IPOSBK(I).LT.0.OR.IPOSBK(I).GT.100) GOTO 80
          ISCPOSBK(NUMSCR, I) = IPOSBK(I)
   60     CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF ALL ITEMS OK THEN PUT THEN IN SCREEN ARRAYS & INCREMENT NO. OF LINES USED
```

```
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      ISCYR (NUMSCR,1) = IYR1-1960
      ISCYR (NUMSCR,2) = IYR2-1960
      ISCINT(NUMSCR)   = INT
      ISCAGE(NUMSCR,1) = IAG1
      ISCAGE(NUMSCR,2) = IAG2
      ISCMS (NUMSCR)   = MS
      ISCIP (NUMSCR)   = IP
      NUMSCR = NUMSCR+1
      GOTO 50
   80 WRITE(6,601)NUMSCR
      STOP
   90 NUMSCR = NUMSCR-1
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C FIRST CHECK TO SEE IF ANY SCREENING IS TO BE DONE IN THIS YEAR
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  100 DO 120 I=1,NUMSCR
          IF(IYR.GE.ISCYR(I,1).AND.IYR.LE.ISCYR(I,2)) GOTO 125
  120     CONTINUE
      RETURN
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF SCREENING IS TO BE DONE EXAMINE EACH ADULT TO SEE IF THEY ARE ELLIGIBLE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  125 DO 500 I=1,ADTNUM
          CALL DECTIM(I,ITIMM,ICLOCK,LSTAT)
          IF(ICLOCK.GT.  0    )        GOTO 500
          CALL DECODE(I,IAG,MS,IP,IST)
          IPT = IP
          IF(IPT.EQ.0) IPT = 1
          IF(IST   .GE.5 )        GOTO 500
          DO 150 J=1,NUMSCR
              IPOL = J
              IF(IAG      .LT.ISCAGE(J,1)   ) GOTO 150
              IF(IAG      .GT.ISCAGE(J,2)   ) GOTO 150
              IF(ISCMS(J).EQ.0              ) GOTO 130
              IF(MS       .NE.ISCMS(J)      ) GOTO 150
  130         IF(ISCIP(J).EQ.0              ) GOTO 140
              IF(IPT      .NE.ISCIP(J)      ) GOTO 150
              GOTO 140
  150         CONTINUE
          GOTO 500
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF SHE IS ELLIGIBLE GENERATE A RANDOM NUMBER TO SEE IF SHE ATTENDED
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  140     CALL RAND (K,100)
          IF(K        .GT.ISCATT(IPOL,IST)) GOTO 400
          ISCTOT = ISCTOT + 1
          ICLOCK = ISCINT(IPOL)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF SHE ATTENDED GENERATE A RANDOM NUMBER TO SEE IF SHE WAS FOUND TO BE +VE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
          CALL RAND (K,1000)
          IF(K        .GT.ISCPOS(IPOL,IST)) GOTO 300
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C         IF TEST IS POSITIVE , UPDATE HER VARIABLES AND
C   INCREMENT THE TRANSITION MATRIX TO TAKE ACCOUNT OF CHANGE OF STATE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
          LSTAT  = IST
          IST    = STPOS
          ITIMM  = 0
          CALL ENCODE (I,IAG,MS,IP,IST)
```

```
            ITRMAT(LSTAT,IST   ) = ITRMAT(LSTAT,IST   ) + 1
            ITRMAT(LSTAT,LSTAT) = ITRMAT(LSTAT,LSTAT) - 1
  300       CALL ENCTIM (I,ITIMM,ICLOCK,LSTAT)
            GO TO 500
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C          DEAL WITH NON-ATTENDERS AT SCREENING
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  400       ISCNA  = ISCNA + 1
            ICLOCK = ISCINT(IPOL)
C.....(Non attenders not offered test until next is due).......
            CALL ENCTIM (I,ITIMM,ICLOCK,LSTAT)
  500       CONTINUE
  601 FORMAT(' ** ERR IN POLICY',I3,' OF SCREEN DATA **')
 1201 FORMAT(80A1)
 1202 FORMAT(2(1X,I4),3(1X,I2),2(1X,I1),6(1X,I3))
 1203 FORMAT(23X,6(1X,I3))
      RETURN
      END
C
```

```
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E     A G E I N G (INFTPC)
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
      COMMON /AGEVAR/ ICHILD(100, 3, 3), IHYST(100),
     1                IMARRY(100, 3, 3), MORT (100),
     1               XPFACT(100, 3)
      COMMON /SUMVAR/ ISTOT(10), ITRMAT(10, 10)
      COMMON /SCRVAR/ ISCYR(20, 2), ISCINT(20)  , ISCAGE(20, 2)  , ISCMS(20),
     1   ISCIP(20) , ISCATT(20, 6), ISCPOS(20, 6), ISCPOSBK(20, 6), IPOSTGT(6),
     2   ISCTOT, ISCNA, ISCGTOT, ISCGNA
C-------------------------------------------------------------------------------
C IFILE ..... CHANNEL NUMBER OF FILE BEING READ
C IKIDZ ..... NUMBER OF FEMALE BIRTHS IN YR THAT WILL BE ADDED TO INFNUM
C INEW ..... POS'N IN NEW ADULT ARRAY, USUALLY LOWER DOWN DUE TO DEATHS
C IPEOPS(I)..... PERSONS AT EACH AGE AT START OF YEAR
C IPEOPE(I)..... PERSONS AT EACH AGE AT END OF YEAR
C PYS(I)..... PERSON YEARS LIVED AT AGE I DURING THE YEAR
C LSTAT ..... FOR ADULTS, THE STATE THEY WERE IN AT START OF CURRENT YR
C-------------------------------------------------------------------------------
      DIMENSION IPEOPS(100), IPEOPE(100), PYS(100)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C EMPTY ARRAYS WHICH ARE USED FOR PERSON YEARS CALCULATION
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 5 I=1, 100
          IPEOPS(I)=0
          IPEOPE(I)=0
          PYS(I)=0
    5     CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF YR 1 OR YR 11 OR 21 THEN READ IN NEW TRANSITION DATA FOR PARA, MARSTAT ETC
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IF(IYR.NE.1.AND.IYR.NE.11.AND.IYR.NE.21) GOTO 100
      IFILE=13
      READ(13, 1301, END=80) (((ICHILD(I, J, K), I=1, 100), K=1, 3), J=1, 3)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CONVERT INCIDENCE FIGURES IN ICHILD TO TRUE PROBABILITIES
C                     AND
C CORRECT PROBABILITIES OF FIRST BIRTH TO ALLOW FOR INFERTILES
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 55 I=1, 100
          DO 50 J=1, 3
            K=1
                  ICHILD(I, J, K) =  (2000 *  ICHILD(I, J, K))
C                                    ----------------------
     1                             /  (2000 +  ICHILD(I, J, K))
            ICHILD(I, J, K) = IFIX(ICHILD(I, J, K) * (1.0/XPFACT(I, J)))
              DO 45 K=2, 3
                  ICHILD(I, J, K) =  (2000 *  ICHILD(I, J, K))
C                                    ----------------------
     1                             /  (2000 +  ICHILD(I, J, K))
   45             CONTINUE
   50           CONTINUE
```

```
   55     CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C READ IN MARITAL STATUS TRANSITION PROBABILITY DISTRIBUTION FROM FOR014
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IFILE=14
      READ(14,1401,END=80)   (IMARRY(I,1,2),I=1,100),
     1                       (IMARRY(I,2,3),I=1,100),
     2                       (IMARRY(I,3,2),I=1,100)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CONVERT MARITAL PROBABILTITY DISTRIBUTION INTO CUMULATIVE TRANSITION MATRIX
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 60 I=1,100
          IMARRY(I,1,1) = 1000 - IMARRY(I,1,2)
          IMARRY(I,1,2) = 1000
          IMARRY(I,1,3) = 1000
          IMARRY(I,2,1) = 0
          IMARRY(I,2,2) = 1000 - IMARRY(I,2,3)
          IMARRY(I,2,3) = 1000
          IMARRY(I,3,1) = 0
          IMARRY(I,3,3) = 1000
   60     CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C READ IN PROBABLITY OF DYING AND OF HAVING HYSTERECTOMY AT EACH AGE YEAR
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IFILE=15
      READ(15,1501,END=80) MORT,IHYST
      GOTO 100
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C PRINT AN ERROR MESSAGE AND STOP IF THERE WAS ANY PROBLEM WITH DATA FILES
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
   80 WRITE(6,601) IFILE
      STOP
  100 IKIDZ=0
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C SET TOTALS FOR EACH  DISEASE STATE TO ZERO PRIOR TO COUNTING
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 135 I=1,10
          ISTOT(I) = 0
  135     CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C EXAMINE EACH ADULT FOR CHANGE IN CHARACTERISTICS AND UPDATE MATRIX IF NEEDED
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      INEW = 0
      DO 500 I=1,ADTNUM
          CALL DECODE(I,IAG,MS,IP,IST)
          CALL DECTIM(I,ITIMM,ICLOCK,LSTAT)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CHECK FOR CANCER DEATHS THIS YEAR
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  140 IF(IST.NE.STHIS) GOTO 150
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C WRITE NEW CANCER DEATHS TO FOR008 AND UPDATE IPEOPS(I)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IF (ITIMM.NE.0) GO TO 480
      WRITE(8,801)IYR,IAG,MS,IP,IST,ITIMM,ICLOCK,LSTAT
      IPEOPS(IAG)=IPEOPS(IAG) + 1
      GO TO 480
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CHECK THAT NO OTHER DEATHS CARRIED OVER FROM LAST YEAR
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  150 IF(IST.NE.STOTH) GOTO 160
```

```
      WRITE(6,610)
      STOP
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C WRITE NEW CANCER CASES TO FOR009
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  160 ISTCA = NUMST - 4
       IF(IST.EQ.ISTCA.AND.ITIMM.EQ.0) GOTO 165
       GOTO 170
  165 WRITE(9,801)IYR,IAG,MS,IP,IST,ITIMM,ICLOCK,LSTAT
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C UPDATE IPEOPS(I) FOR LIVE ADULTS
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  170 IPEOPS(IAG) = IPEOPS(IAG) + 1
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C TEST TO SEE IF HER MARITAL STATUS CHANGES, THIS SECTION MISSED IF SHE IS DEAD
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  180      CALL RAND(K,1000)
           DO 200 J=1,3
                IF(K.GT.IMARRY(IAG,MS,J)) GOTO 200
                MS = J
                GOTO 220
  200           CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF SHE IS NOT DEAD ,CHECK THAT NOT INFERTILE,OR HAD HYSTERECTOMY;
C     IF NEITHER,THEN CHECK TO SEE IF BIRTH OCCURS
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  220      IF(IP .EQ. 0 )                GOTO 300
           IF(IST .EQ. STHYST)           GOTO 400
           CALL RAND(K,1000)
           IF(K.GT.ICHILD(IAG,MS,IP)) GOTO 300
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF SHE HAD ONE THEN TEST TO SEE IF IT WAS FEMALE, INCREMENT IKIDZ IF IT WAS
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
           CALL RAND(K,1000)
           IF(IP.EQ.1.AND.K.GT.483)    GOTO 240
           IF(IP.EQ.2.AND.K.GT.485)    GOTO 240
           IF(IP.EQ.3.AND.K.GT.488)    GOTO 240
           IKIDZ = IKIDZ+1
  240      IF(IP.LT.3) IP=IP+1
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C NOW CHECK TO SEE IF SHE HAS A HYSTERECTOMY, IF SO CHANGE IST, RESET ITIMM,
C  AND INCREMENT THE TRANSITION MATRIX TO TAKE ACCOUNT OF CHANGE OF STATE
C   (N.B. THIS SECTION SKIPPED IF ALREADY HAS HAD HYSTERECTOMY,OR DEAD)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  300      CALL RAND(K,100 000)
           IF(K.GT.IHYST(IAG)) GOTO 400
           LSTAT=IST
           IST=STHYST
           ITIMM=0
           ITRMAT(LSTAT,IST  ) = ITRMAT(LSTAT,IST  ) + 1
           ITRMAT(LSTAT,LSTAT) = ITRMAT(LSTAT,LSTAT) - 1
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C NOW CHECK TO SEE IF SHE HAS DIED OF OTHER CAUSES,IF SO CHANGE IST, RESET
C ITIMM, AND INCREMENT THE TRANSITION MATRIX TO TAKE ACCOUNT OF CHANGE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  400      CALL RAND(K,100 000)
           IF(K.GT.MORT(IAG)) GOTO 450
           LSTAT = IST
           IST   = STOTH
           ITIMM = 0
           ITRMAT(LSTAT,IST  ) = ITRMAT(LSTAT,IST  ) + 1
```

```
          ITRMAT(LSTAT,LSTAT) = ITRMAT(LSTAT,LSTAT) - 1
          GO TO 500
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C UPDATE ARRAY IPEOPE(I) FOR LIVE ADULTS
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  450  IPEOPE(IAG) = IPEOPE(IAG) + 1
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C AGE HER AND UPDATE ICLOCK
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  470     IF( IAG.LT.100  )  IAG    =    IAG + 1
          IF(ICLOCK.GT.0  )  ICLOCK = ICLOCK - 1
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C IF SHE DID NOT DIE OF OTHER CAUSES PUT HER BACK IN THE 'INEW' POS'N IN ARRAY
C               AND INCREMENT ITIMM READY FOR NEXT YEAR
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  480     INEW = INEW + 1
          ITIMM = ITIMM + 1
          CALL ENCODE(INEW,IAG,MS,IP,IST)
          CALL ENCTIM(INEW,ITIMM,ICLOCK,LSTAT)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C GO BACK AND LOOK AT NEXT WOMAN
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  500     CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C GET READY TO LOOK AT INFANTS
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      INFMRT = 0
      MS = 1
      ICLOCK = 0
      LSTAT = 1
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C LOOK AT INFANTS IN 15TH YEAR FOR DEATHS
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
       IPEOPS(15) = INFANT(15)
         NUMDED=0
         IF(INFANT(15).EQ.0) GOTO 700
         DO 520 J=1,INFANT(15)
           IST=1
           CALL RAND(K,100 000)
           IF(K.GT.MORT(15)) GOTO 520
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C FOR EACH DEATH(15TH YR) INCREMENT THE COUNTERS AND ADJUST THE TRANS. MATRIX
C CALCULATE IPEOPE(15)- IE 15 YEAR OLDS WHO SURVIVE THE YEAR
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
           NUMDED          = NUMDED          + 1
           INFMRT          = INFMRT          + 1
           ITRMAT(1,1)     = ITRMAT(1,1)     - 1
           ITRMAT(1,STOTH) = ITRMAT(1,STOTH) + 1
  520      CONTINUE
     IPEOPE(15) = INFANT(15) - NUMDED
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C ADD LIVE INFANTS IN 15TH YEAR TO ADULTS
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      NEWADT=INFANT(15)-NUMDED
      IF(NEWADT.EQ.0) GOTO 600
      INFNUM = INFNUM - NEWADT
      ISTART=INEW+1
      ADTNUM=INEW+NEWADT
      DO 590 I=ISTART,ADTNUM
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CHECK EACH LIVE 15TH YR INDIVL. TO SEE IF SHE IS GOING TO BE FERTILE
```

```
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
          IP = 0
          CALL RAND(K,1000)
          IF(K.LE.INFTPC) GOTO 570
          IP = 1
  570     IAG = 16
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C ENTER LIVE 15TH YEAR INDIVIDUALS AS NEW ADULTS IN 16TH YEAR
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  580     CALL ENCODE(I,IAG,MS,IP,IST)
          CALL ENCTIM(I,IAG,ICLOCK,LSTAT)
  590     CONTINUE
  600   INFANT(15) = 0
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C LOOK AT REST OF INFANTS (IE IN 1ST TO 14TH YEARS)
C FIRST CHECK WITHIN EACH INFANT YEAR AGE GROUP FOR DEATHS
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  700 DO 715 I=1,14
      IPEOPS(I) = INFANT(I)
          NUMDED=0
          IF(INFANT(I).EQ.0) GOTO 715
          DO 710 J=1,INFANT(I)
               IST = 1
               IP = 0
               CALL RAND(K,100 000)
               IF(K.GT.MORT(I)) GOTO 710
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C FOR EACH DEATH INCREMENT THE COUNTERS AND ADJUST THE TRANSITION MATRIX
C CALCULATE PEOPE(I)-IE NUMBER SURVIVING THE YEAR AT EACH AGE
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
               NUMDED           = NUMDED           + 1
               INFMRT           = INFMRT           + 1
               ITRMAT(1,1)      = ITRMAT(1,1)      - 1
               ITRMAT(1,STOTH) = ITRMAT(1,STOTH) + 1
               IST = STOTH
  710          CONTINUE
          INFANT(I)=INFANT(I)-NUMDED
          IPEOPE(I) = INFANT(I)
  715     CONTINUE
        ISTOT(1) = ISTOT(1) + INFNUM + NEWADT - INFMRT
        ISTOT(STOTH) = ISTOT(STOTH) + INFMRT
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CALCULATE STATE TOTALS FROM TRANSITION MATRIX
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
       DO 718 J = 1,NUMST
         ISTOT(J) = 0
         DO 718 I = 1,NUMST
         ISTOT(J) = ISTOT(J) + ITRMAT(I,J)
  718  CONTINUE
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C WRITE OUT THE TRANSITION MATRIX, STATE TOTALS AND TOTAL POPULATION FIGURES
C::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      WRITE(6,602) IYR,(I,I=1,NUMST)
      WRITE(6,603)
      DO 720 I=1,NUMST
          WRITE(6,604) I,(ITRMAT(I,J),J=1,NUMST)
  720     CONTINUE
     ISCGTOT = ISCGTOT + ISCTOT
     ISCGNA  = ISCGNA  + ISCNA
     IOFFERS = ISCTOT  + ISCNA
     IGOFFERS= ISCGTOT + ISCGNA
```

```
      DO 721 I = 1,6
        IPOSTGT(I) = IPOSTGT(I) + ITRMAT(I,STPOS)
721     CONTINUE
      IF(IOFFERS.GT.0) GOTO 722
      WRITE(6,615) ISCTOT
      GO TO 723
722   IATT =(ISCTOT * 100)/IOFFERS
      WRITE(6,605) ISCTOT,IATT
723   IF(IGOFFERS.GT.0) GOTO 724
      WRITE(6,616) ISCGTOT
      GO TO 725
724   IGATT=(ISCGTOT * 100)/IGOFFERS
      WRITE(6,612) ISCGTOT,IGATT
725   WRITE(6,613) (I,I=1,5)
      WRITE(6,614) (IPOSTGT(I),I=1,5)
      ITTPOP = 0
      WRITE(6,606)
      K=NUMST - 2
      DO 740 I=1,K
        ITTPOP = ITTPOP + ISTOT(I)
        IF(I .NE. 1) GOTO 730
        ISTOT(I)=ISTOT(I) + IKIDZ
730     WRITE(6,607)I,ISTOT(I)
740     CONTINUE
      I = NUMST -1
      WRITE(6,607)I,ISTOT(I)
      I = NUMST
      WRITE(6,607)I,ISTOT(I)
      ITTPOP = ITTPOP + IKIDZ
      WRITE(6,608) ITTPOP
      WRITE(6,609) IKIDZ
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C AGE THE LIVE INFANTS(1-14YRS) BY MOVING THEM UP INTO THE NEXT AGE GROUP
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
750   INFNUM = 0
      DO 800 I=1,14
          IFR          = 15-I
          ITO          = 16-I
          INFANT(ITO) = INFANT(IFR)
          INFNUM       = INFNUM + INFANT(ITO)
800       CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C THE NUMBER OF BIRTHS THIS YEAR IS PUT INTO THE FIRST YEAR INFANT AGE GROUP
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      INFANT(1) = IKIDZ
      INFNUM    = INFNUM + IKIDZ
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C CALCULATE PERSON YEARS AT EACH AGE AND WRITE TO FILE FOR010
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      DO 850 I=1,100
        X = FLOAT(IPEOPS(I))
        Y = FLOAT(IPEOPE(I))
        PYS(I) = ( X+Y ) /2
850   CONTINUE
      WRITE(10,1601) IYR,(PYS(I),I=1,10)
      DO 860 J=1,9
        JL=(J*10)+1
        JU=JL+9
        WRITE(10,1602) (PYS(I),I=JL,JU)
860   CONTINUE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
```

```
C RESET NUMBER SCREENED TO ZERO READY FOR NEXT YEARS SCREENEES
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
  950 ISCTOT     = 0
      ISCNA      = 0
      RETURN
  601 FORMAT(' ** FILE SIZE IN AGEING SECTION, FILE',I3' **')
  602 FORMAT(20X,'Y E A R ',I2/20X,'----------'///
     1' FROM STATE'16X,'T O      S T A T E'/10X,10I6)
  603 FORMAT(1X,69(1H-))
  604 FORMAT(I5,5X,10I6)
  605 FORMAT(/' TOTAL SCREENED THIS YEAR ',I8,'(',I3,'% ELLIGIBLE)')
  606 FORMAT(/)
  607 FORMAT(' NUMBER IN STATE ',I2,' ... ',I8)
  608 FORMAT(/' TOTAL POPULATION ..... ',I8)
  609 FORMAT(/' NUMBER OF BIRTHS ..... ',I8///)
  610 FORMAT(/' DEAD SUBJECT IN AGEING SUBROUTINE,LINE 140')
  611 FORMAT(/'ERROR IN IPEOPE(16),AGEING SUBROUTINE,LINE 470')
  612 FORMAT(' TOTAL SCREENED TO DATE   ',I8,'(',I3,'% ELLIGIBLE)')
  613 FORMAT(30X,6(1X,I4))
  614 FORMAT(' TOTAL POSITIVE TESTS TO DATE',1X,5I5)
  615 FORMAT(/' TOTAL SCREENED THIS YEAR ',I8)
  616 FORMAT(' TOTAL SCREENED TO DATE   ',I8)
  801 FORMAT(8I3)
  901 FORMAT(9I3)
 1301 FORMAT(20(1X,I3))
 1401 FORMAT(20(1X,I3))
 1501 FORMAT(10I8)
 1601 FORMAT(1X,I2,1X,10(F6.1))
 1602 FORMAT(4X,10(F6.1))
      END
C
```

```
C*****************************************************************************
C*****************************************************************************
C*****
      S U B R O U T I N E      R A N D   (IRES, IRANGE)
C*****
C*****************************************************************************
C*****************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C THIS IS  ROUTINE FOR GENERATING RANDOM NUMBERS IN A GIVEN RANGE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      INTEGER*4        IR1, IR2
      LOGICAL*1        CALL1 /.TRUE./
      REAL*4           RLIST(0:99)
C
        IF ( CALL1 ) THEN
           CALL1=.FALSE.
           IR1=IFIX(100.*SECNDS(0.))
           DO I=0,99
              RLIST(I)=RAN(IR1)
           END DO
           IR2=IFIX(100.*SECNDS(0.))
        END IF
C
        I=IFIX(100.*RAN(IR2))
        IRES=1+INT(RLIST(I)*IRANGE)
        RLIST(I)=RAN(IR1)
C
        RETURN
        END
C
```

```
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E     E N C O D E (IREC, IAG, MS, IP, IST)
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C PRINT ERROR MESSAGE AND STOP PROGRAM IF WE ARE TRYING TO GO OUTSIDE ARRAY
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IF(IREC.LE.109999) GOTO 50
      WRITE(6,601)
      STOP
   50 ADULT(IREC)=200*(IAG-1)+18*(IST-1)+4*(MS-1)+IP
  601 FORMAT(' ** POPN ARRAY OVERFLOW, RECOMPILE WITH'
     1       ' LARGER ARRAY IF REQUIRED **')
      RETURN
      END
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E     D E C O D E (IREC, IAG, MS, IP, IST)
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
C-------------------------------------------------------------------------------
C IREC ......  INDEX NUMBER OF THE PERSON WHOSE VARIBLES WE WANT
C IVAL ......  THE STORED VALUE IN ADULT(IREC) CONTAINING THE VARIABLES
C-------------------------------------------------------------------------------
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C DIVIDE IVAL BY THE SIZE OF EACH FIELD IN TURN TO GET THEIR VALUES
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IVAL   = ADULT(IREC)
      IAG    = IVAL/200+1
      IVAL   = IVAL-(IAG-1)*200
      IST    = IVAL/18 +1
      IVAL   = IVAL-(IST-1)*18
      MS     = IVAL/4  +1
      IP     = IVAL-(MS-1)*4
      RETURN
      END
C
```

```
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E     E N C T I M (IREC, ITIMM, ICLOCK, LSTAT)
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C ENCODE THE DESIRED WOMAN'S TIME IN STATE, SCREENING CLOCK AND STATE LAST YEAR
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      TIMES(IREC) = 300*ITIMM + 10*(ICLOCK) + LSTAT-1
      RETURN
      END
C*******************************************************************************
C*******************************************************************************
C*****
      S U B R O U T I N E     D E C T I M (IREC, ITIMM, ICLOCK, LSTAT)
C*****
C*******************************************************************************
C*******************************************************************************
      INTEGER POPSZE, STHYST, STPOS, STHIS, STOTH, ADTNUM
      INTEGER ADULT, TIMES, DEAD
      COMMON POPSZE, NUMST, NUMYRS, STHYST, STPOS, STHIS, STOTH, INFNUM
      COMMON ADTNUM, IYR
      COMMON INFANT(15), ADULT(109999), TIMES(109999), DEAD(100)
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C DECODE VALUES USING SIMILAR TECHNIQUE TO THAT IN SUBROUTINE DECODE
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
      IVAL=TIMES(IREC)
      ITIMM=IVAL/300
      IVAL=IVAL-ITIMM*300
      ICLOCK=IVAL/10
      LSTAT=IVAL-ICLOCK*10+1
      RETURN
      END
C<FF>
C*******************************************************************************
C*******************************************************************************
C                       ROUTINES FOR TABULATION
C*******************************************************************************
C*******************************************************************************
C
C*******************************************************************************
C*****
        SUBROUTINE TABINI(TABLE, NDIM, LBND, UBND)
C*****
C*******************************************************************************
        INTEGER     TABLE(1), NDIM, LBND(1), UBND(1)
C
        TABLE(1) = 0
        IF ( NDIM.LT.1 ) GOTO 901
C
        TABLE(2) = 1
C
        DO IDIM = 1, NDIM
           ISIZ = UBND(IDIM)-LBND(IDIM)+1
```

```
            IF ( ISIZ.LT.1 ) GOTO 902
            TABLE(2) = TABLE(2)*ISIZ
            TABLE(2*IDIM+1) = LBND(IDIM)
            TABLE(2*IDIM+2) = ISIZ
         END DO
C
         TABLE(1) = NDIM
C
         DO IDIM = 2*NDIM+2+1,2*NDIM+2+TABLE(2)
            TABLE(IDIM) = 0
         END DO
C
         RETURN
C
901      PAUSE 'NUMBER OF DIMENSION  < 1  IN TABINI'
         RETURN
C
902      PAUSE 'INCONSISTENT DIMENSION  IN TABINI'
         RETURN
C
         END
C*******************************************************************************
C*****
         SUBROUTINE TABVAL(IVAL,TABLE,INDEX)
C*****
C*******************************************************************************
         INTEGER     IVAL,TABLE(1),INDEX(1)
C
         NDIM = TABLE(1)
         IF ( NDIM.LT.1 ) GOTO 901
C
         IOFF = 0
         IMUL = 1
C
         DO IDIM = 1,NDIM
            IND1 = INDEX(IDIM)-TABLE(2*IDIM+1)
            IF ( IND1.LT.0 .OR.  IND1.GE.TABLE(2*IDIM+2) ) GOTO 902
            IOFF = IOFF+IMUL*IND1
            IMUL = IMUL*TABLE(2*IDIM+2)
         END DO
C
         IVAL = TABLE(2*NDIM+3+IOFF)
         RETURN
C
901      PAUSE 'NUMBER OF DIMENSION  < 1  IN TABVAL'
         RETURN
C
902      PAUSE 'SUBSCRIPT OUT OF RANGE IN TABVAL'
         RETURN
C
         END
C*******************************************************************************
C*****
         SUBROUTINE TABADD(IVAL,TABLE,INDEX)
C*****
C*******************************************************************************
         INTEGER     IVAL,TABLE(1),INDEX(1)
C
         NDIM = TABLE(1)
         IF ( NDIM.LT.1 ) GOTO 901
C
```

```
      IOFF = 0
      IMUL = 1
C
      DO IDIM = 1,NDIM
         IND1 = INDEX(IDIM)-TABLE(2*IDIM+1)
         IF ( IND1.LT.0 .OR.  IND1.GE.TABLE(2*IDIM+2) ) GOTO 902
         IOFF = IOFF+IMUL*IND1
         IMUL = IMUL*TABLE(2*IDIM+2)
      END DO
C
      TABLE(2*NDIM+3+IOFF) = TABLE(2*NDIM+3+IOFF) + IVAL
      RETURN
C
901   PAUSE 'NUMBER OF DIMENSION  < 1  IN TABADD'
      RETURN
C
902   PAUSE 'SUBSCRIPT OUT OF RANGE IN TABADD'
      RETURN
C
      END
C*******************************************************************************
C*****
      SUBROUTINE TABOUT(TABLE,UNIT)
C*****
C*******************************************************************************
      INTEGER     TABLE(1),UNIT
C
      INTEGER     INDEX(20)
      CHARACTER   LEAD*100,FORM*100,BUF*20
C
      NDIM = TABLE(1)
      IF ( NDIM.LT.1 ) GOTO 901
C
      FORM = '(2H(*'
      LFOR = 5
      LLEA = 2
      DO IDIM = 2,NDIM
         INDEX(IDIM) = TABLE(2*IDIM+1)
         WRITE (BUF,'(I8)') INDEX(IDIM)
         CALL TRIM(BUF,I1,I2,NC)
         WRITE (BUF,'(I8)') INDEX(IDIM)+TABLE(2*IDIM+2)-1
         CALL TRIM(BUF,I1,I2,I3)
         NC = MAX(NC,I3)
         I3 = 1+INT(LOG10(REAL(NC)))
         WRITE (FORM(LFOR+1:),101) ',1H,,I',NC
101      FORMAT (A,I<I3>)
         LFOR = LFOR+6+I3
         LLEA = LLEA+1+NC
      END DO
      FORM(LFOR+1:) = ',1H))'
      LFOR = LFOR+5
      LLEA = LLEA+1
C
      IOFF = 2*NDIM+2
C
10    WRITE (LEAD,FORM) (INDEX(IDIM),IDIM=2,NDIM)
C
      IF ( TABLE(4).LE.10 ) THEN
         WRITE (UNIT,102) LEAD,(TABLE(I),I=IOFF+1,IOFF+TABLE(4))
      ELSE
         WRITE (UNIT,102) LEAD,(TABLE(I),I=IOFF+1,IOFF+10)
```

```
            WRITE (UNIT,103) (TABLE(I),I=IOFF+11,IOFF+TABLE(4))
         END IF
102      FORMAT (1HO,A<LLEA>,X,10I10)
103      FORMAT (1H ,<LLEA>X,X,10I10)
C
         IOFF = IOFF+TABLE(4)
         IDIM = 1
20       IDIM = IDIM+1
         IF ( IDIM.GT.NDIM ) RETURN
         INDEX(IDIM) = INDEX(IDIM)+1
         IF ( INDEX(IDIM).LT.TABLE(2*IDIM+1)+TABLE(2*IDIM+2) ) GOTO 10
         INDEX(IDIM) = TABLE(2*IDIM+1)
         GOTO 20
C
901      PAUSE 'NUMBER OF DIMENSION  < 1  IN TABOUT'
         RETURN
C
         END
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C        TO SKIP LEADING AND TRAILING BLANKS IN A STRING
C:::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
C
C*******************************************************************************
C*****
         SUBROUTINE      TRIM(STRING,BEG_P,END_P,LENGTH)
C*****
C*******************************************************************************
         CHARACTER*(*)   STRING
         INTEGER         BEG_P,END_P,LENGTH
C
         BEG_P=1
         END_P=LEN(STRING)
         DO WHILE ( STRING(BEG_P:BEG_P).EQ.' '.AND.  BEG_P.LE.END_P )
            BEG_P=BEG_P+1
         END DO
         DO WHILE ( STRING(END_P:END_P).EQ.' '.AND.  BEG_P.LE.END_P )
            END_P=END_P-1
         END DO
         LENGTH=END_P-BEG_P+1
         IF ( LENGTH.EQ.0 ) THEN
            BEG_P=1
            END_P=0
         END IF
         RETURN
         END
```

APPENDIX 5

DATA FILES

FILE1.DAT
FILE2.DAT
FILE3.DAT
FILE4.DAT (part)
FILE11.DAT (part)
FILE12.DAT
FILE13.DAT
FILE14.DAT
FILE15.DAT
FILE33.DAT
FILE92.DAT
FILE93.DAT

```
/MS  PARKIN        FILE1 12-OCT-1983 07:44   LPAO:  12-OCT-1983 07:44   DISK$DIS
/MS  PARKIN        FILE1 12-OCT-1983 07:44   LPAO:  12-OCT-1983 07:44   DISK$DIS
/MS  PARKIN        FILE1 12-OCT-1983 07:44   LPAO:  12-OCT-1983 07:44   DISK$DIS

                    PPPP     AAA    RRRR    K   K    III    N   N
                    P   P   A   A   R   R   K   K     I     N   N
                    P   P   A   A   R   R   K  K      I     NN  N
                    PPPP    A   A   RRRR    KKK       I     N N N
                    P       AAAAA   R R     K  K      I     N  NN
                    P       A   A   R  R    K   K     I     N   N
                    P       A   A   R   R   K   K    III    N   N


'FFFFFFFFF     IIIIII     LL          EEEEEEEEEE       11
'FFFFFFFFF     IIIIII     LL          EEEEEEEEEE       11
'F               II       LL          EE             1111
'F               II       LL          EE             1111
'F               II       LL          EE               11
'F               II       LL          EE               11
'FFFFFFF         II       LL          EEEEEEEE         11
'FFFFFFF         II       LL          EEEEEEEE         11
'F               II       LL          EE               11
'F               II       LL          EE               11
'F               II       LL          EE               11          ....
'F               II       LL          EE               11          ....
'F             IIIIII     LLLLLLLLLL  EEEEEEEEEE     111111        ....
'F             IIIIII     LLLLLLLLLL  EEEEEEEEEE     111111        ....


'DDDDDDD       AAAAAA     TTTTTTTTTT      ;;;;       11        333333    555555
'DDDDDDD       AAAAAA     TTTTTTTTTT      ;;;;       11        333333    555555
'D      DD    AA    AA       TT           ;;;;     1111      33      33  55
'D      DD    AA    AA       TT           ;;;;     1111      33      33  55
'D      DD    AA    AA       TT                      11                33  555555
'D      DD    AA    AA       TT                      11                33  555555
'D      DD    AA    AA       TT           ;;;;       11            33
'D      DD    AA    AA       TT           ;;;;       11            33
'D      DD    AAAAAAAAAA     TT           ;;;;       11              33
'D      DD    AAAAAAAAAA     TT           ;;;;       11              33
'D      DD    AA    AA       TT             ;;       11      33      33  55
'D      DD    AA    AA       TT             ;;       11      33      33  55
'DDDDDDD      AA    AA       TT           ;;       111111      333333      5555
'DDDDDDD      AA    AA       TT           ;;       111111      333333      5555


                    PPPP     AAA    RRRR    K   K    III    N   N
                    P   P   A   A   R   R   K   K     I     N   N
                    P   P   A   A   R   R   K  K      I     NN  N
                    PPPP    A   A   RRRR    KKK       I     N N N
                    P       AAAAA   R R     K  K      I     N  NN
                    P       A   A   R  R    K   K     I     N   N
                    P       A   A   R   R   K   K    III    N   N

'MS  PARKIN        FILE1 12-OCT-1983 07:44   LPAO:  12-OCT-1983 07:44   DISK$DIS
'MS  PARKIN        FILE1 12-OCT-1983 07:44   LPAO:  12-OCT-1983 07:44   DISK$DIS
'MS  PARKIN        FILE1 12-OCT-1983 07:44   LPAO:  12-OCT-1983 07:44   DISK$DIS
```

Size of starting population
Number of states
Years of simulation

0000 ←
9 ←
30 ←

3767	3583	3542	3457	3313	3200	3144	3223	3164	3166
3242	3387	3530	3897	4111	3161	3342	3247	3163	2868
2758	2940	2950	2926	2862	2838	2788	2723	2794	2860
3028	2914	2948	2900	3037	3145	3115	3176	3299	3522
3808	3478	2672	2554	2915	3082	3375	3345	3382	3286
3418	3201	3353	3272	3212	3101	3119	3036	3028	2916
3009	2763	2668	2622	2556	2506	2372	2311	2271	2186
2114	1877	1919	1813	1696	1598	1508	1327	1247	1121
067	879	783	679	595	488	407	309	246	185
145	101	75	53	38	26	18	10	8	5
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	2	4	6	8	10
12	14	15	28	42	68	80	100	125	165
183	216	250	283	317	354	390	420	445	462
478	495	505	514	518	521	523	525	526	527
528	529	530	534	538	542	546	550	560	570
580	580	590	600	610	620	630	640	650	660
670	680	690	700	700	700	700	700	700	700
700	700	700	700	700	700	700	700	700	700

(1)

(2)

Block 1 : Starting age distribution

Block 2 : Starting hysterectomy prevalence (per 10000)

```
VAX/VMS  PARKIN        FILE2 12-OCT-1983 07:44   LPA0:  12-OCT-1983 07:44
VAX/VMS  PARKIN        FILE2 12-OCT-1983 07:44   LPA0:  12-OCT-1983 07:44
VAX/VMS  PARKIN        FILE2 12-OCT-1983 07:44   LPA0:  12-OCT-1983 07:44
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K   III    N   N
```

```
FFFFFFFFFF     IIIIII     LL           EEEEEEEEEE     222222
FFFFFFFFFF     IIIIII     LL           EEEEEEEEEE     222222
FF               II       LL           EE            22      22
FF               II       LL           EE            22      22
FF               II       LL           EE                    22
FF               II       LL           EE                    22
FFFFFFFF         II       LL           EEEEEEEE            22
FFFFFFFF         II       LL           EEEEEEEE            22
FF               II       LL           EE                22
FF               II       LL           EE                22
FF               II       LL           EE              22                ....
FF               II       LL           EE              22                ....
FF             IIIIII     LLLLLLLLLL   EEEEEEEEEE    2222222222         ....
FF             IIIIII     LLLLLLLLLL   EEEEEEEEEE    2222222222         ....
```

```
DDDDDDDD       AAAAAA     TTTTTTTTTT       ;;;;        11          000000
DDDDDDDD       AAAAAA     TTTTTTTTTT       ;;;;        11          000000
DD       DD   AA    AA       TT           ;;;;       1111        00      00
DD       DD   AA    AA       TT           ;;;;       1111        00      00
DD       DD   AA    AA       TT                        11        00    0000
DD       DD   AA    AA       TT                        11        00    0000
DD       DD   AA    AA       TT           ;;;;         11        00  00  00
DD       DD   AA    AA       TT           ;;;;         11        00  00  00
DD       DD   AAAAAAAAAA     TT           ;;;;         11        0000    00
DD       DD   AAAAAAAAAA     TT           ;;;;         11        0000    00
DD       DD   AA    AA       TT             ;;         11        00      00
DD       DD   AA    AA       TT             ;;         11        00      00
DDDDDDDD      AA    AA       TT           ;;          111111      000000
DDDDDDDD      AA    AA       TT           ;;          111111      000000
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K   III    N   N
```

```
VAX/VMS  PARKIN        FILE2 12-OCT-1983 07:44   LPA0:  12-OCT-1983 07:44
VAX/VMS  PARKIN        FILE2 12-OCT-1983 07:44   LPA0:  12-OCT-1983 07:44
VAX/VMS  PARKIN        FILE2 12-OCT-1983 07:44   LPA0:  12-OCT-1983 07:44
```

S	M	FM
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
1000	000	000
972	028	000
934	066	000
900	100	000
830	170	000
719	280	001
559	440	001
420	578	002
337	660	003
276	720	004
235	760	005
183	810	007
157	834	009
146	844	010
135	854	011
126	862	012
117	870	013
109	876	015
103	880	017
102	879	019
100	878	022
099	877	024
098	875	027
098	871	031
098	868	034
097	866	037
097	863	040
097	859	044
098	854	048
099	849	052
101	842	057
103	835	062
105	828	067
108	820	072
111	812	077
115	802	083
118	792	090
122	779	099
126	765	109
129	751	120
133	735	132
136	720	144
138	706	156
139	691	170
140	674	186
141	657	202

Marital composition
of
starting population

(single years of age)

143 634 223
144 609 247
145 585 270
147 561 292
149 537 314
150 515 335
152 493 355
153 471 376
154 448 398
155 422 423
155 395 450
155 366 479
155 338 507
155 314 531
155 290 555
155 290 555
155 270 575
155 250 595
156 229 615
157 210 633
158 190 652
160 170 670
161 152 687
163 134 703
165 117 718
167 101 732
169 086 745
172 071 757
172 071 757
172 071 757
172 071 757
172 071 757
172 071 757
172 071 757
172 071 757
172 071 757
172 071 757
172 071 757
172 071 757

```
VAX/VMS  PARKIN        FILE3 12-OCT-1983 07:45   LPA0:  12-OCT-1983 07:45
VAX/VMS  PARKIN        FILE3 12-OCT-1983 07:45   LPA0:  12-OCT-1983 07:45
VAX/VMS  PARKIN        FILE3 12-OCT-1983 07:45   LPA0:  12-OCT-1983 07:45
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K    III    N   N
```

```
FFFFFFFFFF    IIIIII    LL           EEEEEEEEEE    333333
FFFFFFFFFF    IIIIII    LL           EEEEEEEEEE    333333
FF              II      LL           EE          33      33
FF              II      LL           EE          33      33
FF              II      LL           EE                  33
FF              II      LL           EE                  33
FFFFFFFF        II      LL           EEEEEEEE          33
FFFFFFFF        II      LL           EEEEEEEE          33
FF              II      LL           EE                  33
FF              II      LL           EE                  33
FF              II      LL           EE          33      33      ....
FF              II      LL           EE          33      33      ....
FF            IIIIII    LLLLLLLLLL   EEEEEEEEEE    333333      ....
FF            IIIIII    LLLLLLLLLL   EEEEEEEEEE    333333      ....
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;        11
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;        11
DD      DD   AA    AA      TT          ;;;;      1111
DD      DD   AA    AA      TT          ;;;;      1111
DD      DD   AA    AA      TT                      11
DD      DD   AA    AA      TT                      11
DD      DD   AA    AA      TT          ;;;;        11
DD      DD   AA    AA      TT          ;;;;        11
DD      DD   AAAAAAAAAA    TT          ;;;;        11
DD      DD   AAAAAAAAAA    TT          ;;;;        11
DD      DD   AA    AA      TT            ;;        11
DD      DD   AA    AA      TT            ;;        11
DDDDDDDD     AA    AA      TT          ;;        111111
DDDDDDDD     AA    AA      TT          ;;        111111
```


```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K    III    N   N
```



```
VAX/VMS  PARKIN        FILE3 12-OCT-1983 07:45   LPA0:  12-OCT-1983 07:45
VAX/VMS  PARKIN        FILE3 12-OCT-1983 07:45   LPA0:  12-OCT-1983 07:45
VAX/VMS  PARKIN        FILE3 12-OCT-1983 07:45   LPA0:  12-OCT-1983 07:45
```

AGE	Single		Married			Formerly Married		
	60	NUMBER	IN	1000	THAT	ARE	INFERTILE	
1	1000	0	01000	0	01000	0	0	
2	1000	0	01000	0	01000	0	0	
3	1000	0	01000	0	01000	0	0	
4	1000	0	01000	0	01000	0	0	
5	1000	0	01000	0	01000	0	0	
6	1000	0	01000	0	01000	0	0	
7	1000	0	01000	0	01000	0	0	
8	1000	0	01000	0	01000	0	0	
9	1000	0	01000	0	01000	0	0	
10	1000	0	01000	0	01000	0	0	
11	1000	0	01000	0	01000	0	0	
12	1000	0	01000	0	01000	0	0	
13	1000	0	01000	0	01000	0	0	
14	1000	0	01000	0	01000	0	0	
15	1000	0	01000	0	01000	0	0	
16	990	10	01000	0	01000	0	0	
17	990	10	0 667	333	01000	0	0	
18	990	10	0 571	410	191000	0	0	
19	980	20	0 564	396	401000	0	0	
20	970	30	0 560	370	701000	0	0	
21	970	30	0 538	356	106 500	500	0	
22	970	30	0 514	347	139 333	333	334	
23	970	30	0 462	356	182 400	400	200	
24	970	30	0 408	359	233 250	500	250	
25	960	40	0 358	354	288 333	417	250	
26	950	50	0 309	343	348 344	375	281	
27	920	70	10 266	329	405 316	368	316	
28	920	70	10 239	326	435 273	364	363	
29	920	70	10 204	297	499 269	346	385	
30	910	80	10 184	281	535 276	345	379	
31	920	70	10 167	267	566 250	333	417	
32	910	80	10 155	257	588 237	329	434	
33	900	90	10 146	249	605 238	333	429	
34	890	100	10 142	243	615 234	319	447	
35	890	100	10 138	242	620 226	321	453	
36	890	100	10 133	241	626 222	317	461	
37	890	100	10 131	240	629 200	343	457	
38	890	100	10 128	241	631 213	312	475	
39	890	100	10 127	243	630 213	319	468	
40	890	100	10 125	244	631 196	330	474	
41	890	100	10 126	248	626 199	331	470	
42	890	100	10 125	247	628 191	324	485	
43	890	100	10 128	247	625 197	308	495	
44	890	100	10 132	250	618 185	311	504	
45	890	100	10 139	255	606 196	304	500	
46	890	100	10 143	254	603 192	299	509	
47	890	100	10 145	255	600 182	291	527	
48	890	100	10 155	259	586 186	288	526	
49	890	100	10 162	263	575 198	289	513	
50	890	100	10 169	264	567 192	282	526	
51	890	100	10 196	271	533 203	273	524	
52	890	100	10 196	271	533 203	273	524	
53	890	100	10 196	271	533 203	273	524	
54	890	100	10 196	271	533 203	273	524	
55	890	100	10 196	271	533 203	273	524	
56	890	100	10 229	266	505 215	258	527	
57	890	100	10 229	266	505 215	258	527	
58	890	100	10 229	266	505 215	258	527	
59	890	100	10 229	266	505 215	258	527	
60	890	100	10 229	266	505 215	258	527	

For each M.S. column figures are no. per 1000 of parity 0,1,2+ (starting population)

61	890	100	10	239	234	417	205	236	559
62	890	100	10	239	234	417	205	236	559
63	890	100	10	239	234	417	205	236	559
64	890	100	10	239	234	417	205	236	559
65	890	100	10	239	234	417	205	236	559
66	890	100	10	233	234	543	190	216	594
67	890	100	10	233	234	543	190	216	594
68	890	100	10	233	234	543	190	216	594
69	890	100	10	233	234	543	190	216	594
70	890	100	10	233	234	543	190	216	594
71	890	100	10	227	204	569	178	199	623
72	890	100	10	227	204	569	178	199	623
73	890	100	10	227	204	569	178	199	623
74	890	100	10	227	204	569	178	199	623
75	890	100	10	227	204	569	178	199	623
76	890	100	10	217	189	594	164	180	656
77	890	100	10	217	189	594	164	180	656
78	890	100	10	217	189	594	164	180	656
79	890	100	10	217	189	594	164	180	656
80	890	100	10	217	189	594	164	180	656
81	890	100	10	210	174	616	151	159	690
82	890	100	10	210	174	616	151	159	690
83	890	100	10	210	174	616	151	159	690
84	890	100	10	210	174	616	151	159	690
85	890	100	10	210	174	616	151	159	690
86	890	100	10	210	174	616	151	159	690
87	890	100	10	210	174	616	151	159	690
88	890	100	10	210	174	616	151	159	690
89	890	100	10	210	174	616	151	159	690
90	890	100	10	210	174	616	151	159	690
91	890	100	10	210	174	616	151	159	690
92	890	100	10	210	174	616	151	159	690
93	890	100	10	210	174	616	151	159	690
94	890	100	10	210	174	616	151	159	690
95	890	100	10	210	174	616	151	159	690
96	890	100	10	210	174	616	151	159	690
97	890	100	10	210	174	616	151	159	690
98	890	100	10	210	174	616	151	159	690
99	890	100	10	210	174	616	151	159	690
00	890	100	10	210	174	616	151	159	690

```
VAX/VMS  PARKIN        FILE4 12-OCT-1983 07:45    LPA0:  12-OCT-1983 07:46
VAX/VMS  PARKIN        FILE4 12-OCT-1983 07:45    LPA0:  12-OCT-1983 07:46
VAX/VMS  PARKIN        FILE4 12-OCT-1983 07:45    LPA0:  12-OCT-1983 07:46
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K    I     N   N
P   P   A   A   R   R   K  K     I     NN  N
PPPP    A   A   RRRR    KKK      I     N N N
P       AAAAA   R R     K  K     I     N  NN
P       A   A   R  R    K   K    I     N   N
P       A   A   R   R   K   K   III    N   N
```

```
FFFFFFFFFF    IIIIII    LL          EEEEEEEEEE   44    44
FFFFFFFFFF    IIIIII    LL          EEEEEEEEEE   44    44
FF              II      LL          EE           44    44
FF              II      LL          EE           44    44
FF              II      LL          EE           44    44
FF              II      LL          EE           44    44
FFFFFFFF        II      LL          EEEEEEEE     4444444444
FFFFFFFF        II      LL          EEEEEEEE     4444444444
FF              II      LL          EE                44
FF              II      LL          EE                44
FF              II      LL          EE                44          ....
FF              II      LL          EE                44          ....
FF            IIIIII    LLLLLLLLLL  EEEEEEEEEE        44          ....
FF            IIIIII    LLLLLLLLLL  EEEEEEEEEE        44          ....
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT     ;;;;       11        000000
DDDDDDDD      AAAAAA    TTTTTTTTTT     ;;;;       11        000000
DD      DD   AA    AA      TT          ;;;;     1111       00      00
DD      DD   AA    AA      TT          ;;;;     1111       00      00
DD      DD   AA    AA      TT                     11       00    0000
DD      DD   AA    AA      TT                     11       00    0000
DD      DD   AA    AA      TT          ;;;;       11       00  00  00
DD      DD   AA    AA      TT          ;;;;       11       00  00  00
DD      DD   AAAAAAAAAA    TT          ;;;;       11       0000    00
DD      DD   AAAAAAAAAA    TT          ;;;;       11       0000    00
DD      DD   AA    AA      TT            ;;       11       00      00
DD      DD   AA    AA      TT            ;;       11       00      00
DDDDDDDD     AA    AA      TT          ;;       111111       000000
DDDDDDDD     AA    AA      TT          ;;       111111       000000
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K    I     N   N
P   P   A   A   R   R   K  K     I     NN  N
PPPP    A   A   RRRR    KKK      I     N N N
P       AAAAA   R R     K  K     I     N  NN
P       A   A   R  R    K   K    I     N   N
P       A   A   R   R   K   K   III    N   N
```

```
VAX/VMS  PARKIN        FILE4 12-OCT-1983 07:45    LPA0:  12-OCT-1983 07:46
VAX/VMS  PARKIN        FILE4 12-OCT-1983 07:45    LPA0:  12-OCT-1983 07:46
VAX/VMS  PARKIN        FILE4 12-OCT-1983 07:45    LPA0:  12-OCT-1983 07:46
```

STATE 1	2	3	4	5	PARA	MS	AGE
10000	0	0	0	0			
10000	0	0	0	0			
10000	0	0	0	0			
10000	0	0	0	0			
10000	0	0	0	0			
10000	0	0	0	0			
10000	0	0	0	0			15
10000	0	0	0	0			
10000	0	0	0	0			
10000	0	0	0	0			
10000	0	0	0	0			
9959	39	2	0	0			
9957	41	2	0	0			
9954	44	2	0	0			
9956	42	2	0	0			
9954	44	2	0	0			16
9950	47	3	0	0			
9928	68	4	0	0			
9922	74	4	0	0			
9917	78	5	0	0			
9959	39	2	0	0	0		
9957	41	2	0	0	1	S	
9954	44	2	0	0	2+		
9956	42	2	0	0	0		17
9954	44	2	0	0	1	M	
9950	47	3	0	0	2+		
9928	68	4	0	0	0		
9922	74	4	0	0	1	FM	
9917	78	5	0	0	2+		
9959	39	2	0	0			
9957	41	2	0	0			
9954	44	2	0	0			
9956	42	2	0	0			
9954	44	2	0	0			18
9950	47	3	0	0			
9928	68	4	0	0			
9922	74	4	0	0			
9917	78	5	0	0			
9959	39	2	0	0			
9957	41	2	0	0			
9954	44	2	0	0			
9956	42	2	0	0			19
9954	44	2	0	0			
9950	47	3	0	0			
9928	68	4	0	0			
9922	74	4	0	0			
9917	78	5	0	0			
9960	38	2	0	0			
9958	40	2	0	0			
9955	43	2	0	0			
9957	41	2	0	0			
9955	43	2	0	0			20
9951	46	3	0	0			
9930	66	4	0	0			
9924	72	4	0	0			
9919	76	5	0	0			
9869	115	16	0	0			
9862	121	17	0	0			
9853	129	18	0	0			

9642	222	128	5	3	
9822	111	64	2	1	
9813	117	67	2	1	
9800	125	72	2	1	
9809	119	69	2	1	
9798	126	73	2	1	35
9784	134	77	3	2	
9691	192	111	4	2	
9662	210	121	4	3	
9642	222	128	5	3	
9821	92	77	4	6	
9813	96	80	4	7	
9800	103	86	4	7	
9808	99	82	4	7	36
9798	104	87	4	7	
9784	111	92	5	8	
9690	159	133	7	11	
9663	173	145	7	12	
9643	183	153	8	13	
9822	92	76	4	6	
9813	96	80	4	7	
9801	103	85	4	7	
9809	99	81	4	7	37
9799	104	86	4	7	
9785	111	91	5	8	
9692	159	131	7	11	
9665	173	143	7	12	
9645	183	151	8	13	
9821	92	77	4	6	
9813	96	80	4	7	
9800	103	86	4	7	38
9808	99	82	4	7	
9798	104	87	4	7	
9784	111	92	5	8	
9690	159	133	7	11	
9663	173	145	7	12	
9643	183	153	8	13	
9822	92	76	4	6	
9813	96	80	4	7	
9801	103	85	4	7	
9809	99	81	4	7	39
9799	104	86	4	7	
9785	111	91	5	8	
9692	159	131	7	11	
9665	173	143	7	12	
9645	183	151	8	13	
9824	91	75	4	6	
9815	95	79	4	7	
9803	102	84	4	7	
9810	98	81	4	7	40
9801	103	85	4	7	
9787	110	90	5	8	
9694	158	130	7	11	
9667	172	142	7	12	
9647	182	150	8	13	
9834	74	74	6	12	
9824	78	78	7	13	
9813	83	83	7	14	
9820	80	80	7	13	
9811	84	84	7	14	
9799	89	89	8	15	

9839	62	74	7	18	
9829	66	78	8	19	
9754	95	113	11	27	
9731	104	123	12	30	
9716	110	130	13	31	
9859	55	65	6	15	
9851	58	68	7	16	
9841	62	73	7	17	
9847	59	70	7	17	49
9839	62	74	7	18	
9829	66	78	8	19	
9754	95	113	11	27	
9731	104	123	12	30	
9716	110	130	13	31	
9859	55	65	6	15	
9851	58	68	7	16	
9841	62	73	7	17	
9847	59	70	7	17	50
9839	62	74	7	18	
9829	66	78	8	19	
9754	95	113	11	27	
9731	104	123	12	30	
9716	110	130	13	31	
9870	50	56	7	17	
9865	52	58	7	18	
9855	56	62	8	19	
9860	54	60	8	18	51
9853	57	63	8	19	
9843	60	67	9	21	
9773	87	97	13	30	
9754	94	105	14	33	
9739	100	111	15	35	
9870	50	56	7	17	
9865	52	58	7	18	
9855	56	62	8	19	52
9860	54	60	8	18	
9853	57	63	8	19	
9843	60	67	9	21	
9773	87	97	13	30	
9754	94	105	14	33	
9739	100	111	15	35	
9872	49	55	7	17	
9866	51	58	7	18	
9856	55	62	8	19	
9862	53	59	8	18	53
9855	56	62	8	19	
9845	59	66	9	21	
9777	85	95	13	30	
9756	93	104	14	33	
9742	98	110	15	35	
9872	49	55	7	17	
9866	51	58	7	18	
9856	55	62	8	19	
9862	53	59	8	18	54
9855	56	62	8	19	
9845	59	66	9	21	
9777	85	95	13	30	
9756	93	104	14	33	
9742	98	110	15	35	
9872	49	55	7	17	
9866	51	58	7	18	

```
VAX/VMS  PARKIN        FILE11M 12-OCT-1983 07:46   LPA0:  12-OCT-1983 07:49
VAX/VMS  PARKIN        FILE11M 12-OCT-1983 07:46   LPA0:  12-OCT-1983 07:49
VAX/VMS  PARKIN        FILE11M 12-OCT-1983 07:46   LPA0:  12-OCT-1983 07:49
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K   III    N   N
```

```
FFFFFFFFFF    IIIIII    LL           EEEEEEEEEE      11          11
FFFFFFFFFF    IIIIII    LL           EEEEEEEEEE      11          11
FF              II      LL           EE            1111        1111
FF              II      LL           EE            1111        1111
FF              II      LL           EE              11          11
FF              II      LL           EE              11          11
FFFFFFFF        II      LL           EEEEEEEE        11          11
FFFFFFFF        II      LL           EEEEEEEE        11          11
FF              II      LL           EE              11          11
FF              II      LL           EE              11          11
FF              II      LL           EE              11          11
FF              II      LL           EE              11          11
FF            IIIIII    LLLLLLLLLL   EEEEEEEEEE    111111      111111
FF            IIIIII    LLLLLLLLLL   EEEEEEEEEE    111111      111111
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;      222222
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;      222222
DD      DD   AA    AA      TT          ;;;;     22      22
DD      DD   AA    AA      TT          ;;;;     22      22
DD      DD   AA    AA      TT                           22
DD      DD   AA    AA      TT                           22
DD      DD   AA    AA      TT          ;;;;          22
DD      DD   AA    AA      TT          ;;;;          22
DD      DD   AAAAAAAAAA    TT          ;;;;        22
DD      DD   AAAAAAAAAA    TT          ;;;;        22
DD      DD   AA    AA      TT            ;;      22
DD      DD   AA    AA      TT            ;;      22
DDDDDDDD     AA    AA      TT          ;;        2222222222
DDDDDDDD     AA    AA      TT          ;;        2222222222
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K   III    N   N
```

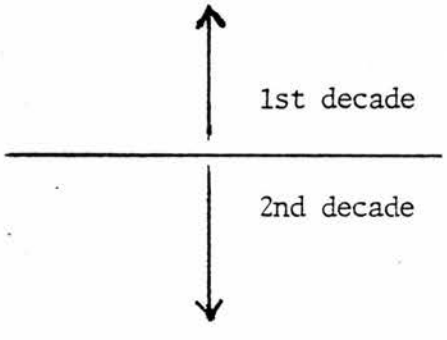
```
VAX/VMS  PARKIN        FILE11M 12-OCT-1983 07:46   LPA0:  12-OCT-1983 07:49
VAX/VMS  PARKIN        FILE11M 12-OCT-1983 07:46   LPA0:  12-OCT-1983 07:49
VAX/VMS  PARKIN        FILE11M 12-OCT-1983 07:46   LPA0:  12-OCT-1983 07:49
```

1	2	3	4	5	6	7	8	9
1	2	16	20	1	1	0	99	0.163848
1	2	16	20	2	1	0	99	0.260401
1	2	16	20	3	1	0	99	0.280883
1	2	16	20	1	2	0	99	0.178477
1	2	16	20	2	2	0	99	0.286734
1	2	16	20	3	2	0	99	0.310141
1	2	16	20	1	3	0	99	0.403769
1	2	16	20	2	3	0	99	0.643689
1	2	16	20	3	3	0	99	0.696355
1	2	21	25	1	1	0	99	0.390435
1	2	21	25	2	1	0	99	0.620513
1	2	21	25	3	1	0	99	0.669318
1	2	21	25	1	2	0	99	0.425296
1	2	21	25	2	2	0	99	0.683262
1	2	21	25	3	2	0	99	0.739038
1	2	21	25	1	3	0	99	0.962144
1	2	21	25	2	3	0	99	1.533853
1	2	21	25	3	3	0	99	1.659350
1	2	26	30	1	1	0	99	0.286135
1	2	26	30	2	1	0	99	0.454751
1	2	26	30	3	1	0	99	0.490518
1	2	26	30	1	2	0	99	0.311683
1	2	26	30	2	2	0	99	0.500737
1	2	26	30	3	2	0	99	0.541613
1	2	26	30	1	3	0	99	0.705119
1	2	26	30	2	3	0	99	1.124103
1	2	26	30	3	3	0	99	1.216076
1	2	31	35	1	1	0	99	0.218352
1	2	31	35	2	1	0	99	0.347023
1	2	31	35	3	1	0	99	0.374317
1	2	31	35	1	2	0	99	0.237848
1	2	31	35	2	2	0	99	0.382116
1	2	31	35	3	2	0	99	0.413309
1	2	31	35	1	3	0	99	0.538081
1	2	31	35	2	3	0	99	0.857811
1	2	31	35	3	3	0	99	0.927995
1	2	36	40	1	1	0	99	0.177995
1	2	36	40	2	1	0	99	0.282885
1	2	36	40	3	1	0	99	0.305135
1	2	36	40	1	2	0	99	0.193888
1	2	36	40	2	2	0	99	0.311492
1	2	36	40	3	2	0	99	0.336920
1	2	36	40	1	3	0	99	0.438631
1	2	36	40	2	3	0	99	0.699267
1	2	36	40	3	3	0	99	0.756480
1	2	41	45	1	1	0	99	0.141632
1	2	41	45	2	1	0	99	0.225094
1	2	41	45	3	1	0	99	0.242798
1	2	41	45	1	2	0	99	0.154278
1	2	41	45	2	2	0	99	0.247856
1	2	41	45	3	2	0	99	0.268089
1	2	41	45	1	3	0	99	0.349022
1	2	41	45	2	3	0	99	0.556411
1	2	41	45	3	3	0	99	0.601936
1	2	46	50	1	1	0	99	0.105410
1	2	46	50	2	1	0	99	0.167527
1	2	46	50	3	1	0	99	0.180704
1	2	46	50	1	2	0	99	0.114822
1	2	46	50	2	2	0	99	0.184468
1	2	46	50	3	2	0	99	0.199527
1	2	46	50	1	3	0	99	0.259761

Columns

1 from state
2 to state
3
4) between ages
5 parity
6 marital state
7
8) between state (1) duration
9 transfer rate

```
 1   2   46 50 2 3 0 99    0.414112
 1   2   46 50 3 3 0 99    0.447994
 1   2   51100 1 1 0 99    0.053334
 1   2   51100 2 1 0 99    0.084762
 1   2   51100 3 1 0 99    0.091429
 1   2   51100 1 2 0 99    0.058095
 1   2   51100 2 2 0 99    0.093334
 1   2   51100 3 2 0 99    0.100953
 1   2   51100 1 3 0 99    0.131429
 1   2   51100 2 3 0 99    0.209524
 1   2   51100 3 3 0 99    0.226667
 2   1   16 50 0 0 0 99    25.000000
 2   1   51100 0 0 0 99    12.500000
 2   3   16100 0 0 0 99     5.000000
 3   2   16 50 0 0 0 99     1.000000
 3   2   51100 0 0 0 99     0.500000
 3   4   16 20 0 0 0 99     0.500000
 3   4   21 25 0 0 0 99     1.000000
 3   4   26 30 0 0 0 99     1.500000
 3   4   31 35 0 0 0 99     2.000000
 3   4   36 40 0 0 0 99     3.000000
 3   4   41 50 0 0 0 99     5.000000
 3   4   51 60 0 0 0 99     7.000000
 3   4   61 70 0 0 0 99     8.000000
 3   4   71 80 0 0 0 99     9.000000
 3   4   81100 0 0 0 99    10.000000
 4   5   16100 0 0 1  1     0.000000
 4   5   16100 0 0 2 99   100.000000
 5   8   16 30 0 0 1  1    10.000000
 5   8   16 30 0 0 2  3     4.000000
 5   8   16 30 0 0 4  5     2.000000
 5   8   31 40 0 0 1  1    12.000000
 5   8   31 40 0 0 2  3     5.000000
 5   8   31 40 0 0 4  5     3.000000
 5   8   41 50 0 0 1  1    18.000000
 5   8   41 50 0 0 2  3     8.000000
 5   8   41 50 0 0 4  5     4.000000
 5   8   51 60 0 0 1  1    22.000000
 5   8   51 60 0 0 2  3    12.000000
 5   8   51 60 0 0 4  5     5.000000
 5   8   61 70 0 0 1  1    27.000000
 5   8   61 70 0 0 2  3    14.000000
 5   8   61 70 0 0 4  5     6.000000
 5   8   71 80 0 0 1  1    41.000000
 5   8   71 80 0 0 2  3    18.000000
 5   8   71 80 0 0 4  5     6.000000
 5   8   81100 0 0 1  1    55.000000
 5   8   81100 0 0 2  3    20.000000
 5   8   81100 0 0 4  5     6.000000
 5   8   16100 0 0 6 99     2.000000
/
 1   2   16 20 1 1 0 99    0.163848
 1   2   16 20 2 1 0 99    0.260401
 1   2   16 20 3 1 0 99    0.280883
 1   2   16 20 1 2 0 99    0.178477
 1   2   16 20 2 2 0 99    0.286734
 1   2   16 20 3 2 0 99    0.310141
 1   2   16 20 1 3 0 99    0.403769
 1   2   16 20 2 3 0 99    0.643689
 1   2   16 20 3 3 0 99    0.696355
 1   2   21 25 1 1 0 99    0.390435
```



```
VAX/VMS  SCRATCH       FILE12 13-OCT-1983 08:28   LPA0:  13-OCT-1983 08:34
VAX/VMS  SCRATCH       FILE12 13-OCT-1983 08:28   LPA0:  13-OCT-1983 08:34
VAX/VMS  SCRATCH       FILE12 13-OCT-1983 08:28   LPA0:  13-OCT-1983 08:34
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
FFFFFFFFFF    IIIIII    LL           EEEEEEEEEE      11        222222
FFFFFFFFFF    IIIIII    LL           EEEEEEEEEE      11        222222
FF              II      LL           EE            1111      22      22
FF              II      LL           EE            1111      22      22
FF              II      LL           EE              11              22
FF              II      LL           EE              11              22
FFFFFFFF        II      LL           EEEEEEEE        11            22
FFFFFFFF        II      LL           EEEEEEEE        11            22
FF              II      LL           EE              11          22
FF              II      LL           EE              11          22
FF              II      LL           EE              11        22
FF              II      LL           EE              11        22
FF            IIIIII    LLLLLLLLLL   EEEEEEEEEE    111111    2222222222
FF            IIIIII    LLLLLLLLLL   EEEEEEEEEE    111111    2222222222
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;      222222      666666
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;      222222      666666
DD      DD   AA    AA      TT            ;;;;    22      22  66
DD      DD   AA    AA      TT            ;;;;    22      22  66
DD      DD   AA    AA      TT                            22  66
DD      DD   AA    AA      TT                            22  66
DD      DD   AA    AA      TT            ;;;;        22      66666666
DD      DD   AA    AA      TT            ;;;;        22      66666666
DD      DD   AAAAAAAAAA    TT            ;;;;      22        66      66
DD      DD   AAAAAAAAAA    TT            ;;;;      22        66      66
DD      DD   AA    AA      TT              ;;    22          66      66
DD      DD   AA    AA      TT              ;;    22          66      66
DDDDDDDD     AA    AA      TT            ;;      2222222222    666666
DDDDDDDD     AA    AA      TT            ;;      2222222222    666666
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
VAX/VMS  SCRATCH       FILE12 13-OCT-1983 08:28   LPA0:  13-OCT-1983 08:34
VAX/VMS  SCRATCH       FILE12 13-OCT-1983 08:28   LPA0:  13-OCT-1983 08:34
VAX/VMS  SCRATCH       FILE12 13-OCT-1983 08:28   LPA0:  13-OCT-1983 08:34
```

STATE

```
                                        1    2    3    4
1961 1990 01 36 36 0 0                 60   60   60   60 ← % in each state who attend
                                        5  700  700  700 ← No per 1000 found positive (move to
                                      100    8    4   00 ← STPOS)
1961 1990 01 41 41 0 0                 55   55   55   55 ← % who return from STPOS
                                        5  700  700  700
                                      100    8    4   00
1961 1990 01 46 46 0 0                 50   50   50   50
                                        5  700  700  700
                                      100    8    4   00
1961 1990 01 51 51 0 0                 45   45   45   45
                                        5  700  700  700
                                      100    8    4   00
1961 1990 01 56 56 0 0                 40   40   40   40
                                        5  700  700  700
                                      100    8    4   00
1961 1990 01 61 61 0 0                 35   35   35   35
                                        5  700  700  700
                                      100    8    4   00
1961 1990 01 66 66 0 0                 30   30   30   30
                                        5  700  700  700
                                      100    8    4   00
//
```

Parity eligible)
) 0 = all
M.S. eligible)

Ages for screening

Interval between offers

Years of policy

```
X/VMS  PARKIN        FILE13 12-OCT-1983 07:47   LPA0:  12-OCT-1983 07:50   DISK$I
X/VMS  PARKIN        FILE13 12-OCT-1983 07:47   LPA0:  12-OCT-1983 07:50   DISK$I
X/VMS  PARKIN        FILE13 12-OCT-1983 07:47   LPA0:  12-OCT-1983 07:50   DISK$I


                    PPPP     AAA   RRRR   K   K   III   N   N
                    P   P   A   A  R   R  K   K   I    N   N
                    P   P   A   A  R   R  K  K    I    NN  N
                    PPPP    A   A  RRRR   KKK     I    N N N
                    P       AAAAA  R R    K  K    I    N  NN
                    P       A   A  R  R   K   K   I    N   N
                    P       A   A  R   R  K   K  III   N   N


FFFFFFFFFF    IIIIII    LL          EEEEEEEEEE     11       333333
FFFFFFFFFF    IIIIII    LL          EEEEEEEEEE     11       333333
FF              II      LL          EE            1111     33     33
FF              II      LL          EE            1111     33     33
FF              II      LL          EE              11             33
FF              II      LL          EE              11             33
FFFFFFFF        II      LL          EEEEEEEE        11           33
FFFFFFFF        II      LL          EEEEEEEE        11           33
FF              II      LL          EE              11             33
FF              II      LL          EE              11             33
FF              II      LL          EE              11     33      33
FF              II      LL          EE              11     33      33
FF            IIIIII    LLLLLLLLLL  EEEEEEEEEE    111111     333333
FF            IIIIII    LLLLLLLLLL  EEEEEEEEEE    111111     333333


DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;        11
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;        11
DD      DD   AA    AA      TT          ;;;;       1111
DD      DD   AA    AA      TT          ;;;;       1111
DD      DD   AA    AA      TT                       11
DD      DD   AA    AA      TT                       11
DD      DD   AA    AA      TT          ;;;;         11
DD      DD   AA    AA      TT          ;;;;         11
DD      DD   AAAAAAAAAA    TT          ;;;;         11
DD      DD   AAAAAAAAAA    TT          ;;;;         11
DD      DD   AA    AA      TT            ;;         11
DD      DD   AA    AA      TT            ;;         11
DDDDDDDD     AA    AA      TT          ;;         111111
DDDDDDDD     AA    AA      TT          ;;         111111


                    PPPP     AAA   RRRR   K   K   III   N   N
                    P   P   A   A  R   R  K   K   I    N   N
                    P   P   A   A  R   R  K  K    I    NN  N
                    PPPP    A   A  RRRR   KKK     I    N N N
                    P       AAAAA  R R    K  K    I    N  NN
                    P       A   A  R  R   K   K   I    N   N
                    P       A   A  R   R  K   K  III   N   N


/VMS   PARKIN        FILE13 12-OCT-1983 07:47   LPA0:  12-OCT-1983 07:50   DISK$I
/VMS   PARKIN        FILE13 12-OCT-1983 07:47   LPA0:  12-OCT-1983 07:50   DISK$I
/VMS   PARKIN        FILE13 12-OCT-1983 07:47   LPA0:  12-OCT-1983 07:50   DISK$I
```

One block per decade - Marital status (L) + Parity (R)
Rates of fertility by single years (per 1000)

00	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	005	008	011	014	017
21	025	029	033	037	041	044	048	046	044	044	042	041	037	033	029	026	023	019	016	
12	009	006	003	001	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	
00	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	
00	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	
00	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	005	008	011	014	017
21	025	029	033	037	041	044	048	046	044	044	042	041	037	033	029	026	023	019	016	
12	009	006	003	001	000	000	000	000	000	000	000	000	000	000	000	000	000	000	000	
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Decades 1 - 3 (R)

Rates of marriage (M) widowhood/divorce (w.d.) and remarriage (R)

Single years of age (per 1000)

```
X/VMS  PARKIN        FILE15 12-OCT-1983 07:48   LPA0:  12-OCT-1983 07:51   DISK$D
X/VMS  PARKIN        FILE15 12-OCT-1983 07:48   LPA0:  12-OCT-1983 07:51   DISK$D
X/VMS  PARKIN        FILE15 12-OCT-1983 07:48   LPA0:  12-OCT-1983 07:51   DISK$D

                    PPPP     AAA    RRRR    K   K    III    N   N
                    P   P   A   A   R   R   K   K     I     N   N
                    P   P   A   A   R   R   K  K      I     NN  N
                    PPPP    A   A   RRRR    KKK       I     N N N
                    P       AAAAA   R R     K  K      I     N  NN
                    P       A   A   R  R    K   K     I     N   N
                    P       A   A   R   R   K   K    III    N   N

FFFFFFFFFF     IIIIII     LL          EEEEEEEEEE      11      5555555555
FFFFFFFFFF     IIIIII     LL          EEEEEEEEEE      11      5555555555
FF               II       LL          EE            1111      55
FF               II       LL          EE            1111      55
FF               II       LL          EE              11      555555
FF               II       LL          EE              11      555555
FFFFFFFF         II       LL          EEEEEEEE        11            55
FFFFFFFF         II       LL          EEEEEEEE        11            55
FF               II       LL          EE              11              55
FF               II       LL          EE              11              55
FF               II       LL          EE              11      55      55
FF               II       LL          EE              11      55      55
FF             IIIIII     LLLLLLLLLL  EEEEEEEEEE    111111      555555
FF             IIIIII     LLLLLLLLLL  EEEEEEEEEE    111111      555555

DDDDDDDD       AAAAAA     TTTTTTTTTT      ;;;;        11        000000      00(
DDDDDDDD       AAAAAA     TTTTTTTTTT      ;;;;        11        000000      00(
DD       DD   AA    AA       TT          ;;;;      1111      00      00   00
DD       DD   AA    AA       TT          ;;;;      1111      00      00   00
DD       DD   AA    AA       TT                      11      00    0000   00
DD       DD   AA    AA       TT                      11      00    0000   00
DD       DD   AA    AA       TT          ;;;;        11      00  00  00   00  (
DD       DD   AA    AA       TT          ;;;;        11      00  00  00   00  (
DD       DD   AAAAAAAAAA     TT          ;;;;        11      0000    00   0000
DD       DD   AAAAAAAAAA     TT          ;;;;        11      0000    00   0000
DD       DD   AA    AA       TT            ;;        11      00      00   00
DD       DD   AA    AA       TT            ;;        11      00      00   00
DDDDDDDD      AA    AA       TT          ;;        111111      000000      00(
DDDDDDDD      AA    AA       TT          ;;        111111      000000      00(

                    PPPP     AAA    RRRR    K   K    III    N   N
                    P   P   A   A   R   R   K   K     I     N   N
                    P   P   A   A   R   R   K  K      I     NN  N
                    PPPP    A   A   RRRR    KKK       I     N N N
                    P       AAAAA   R R     K  K      I     N  NN
                    P       A   A   R  R    K   K     I     N   N
                    P       A   A   R   R   K   K    III    N   N

/VMS   PARKIN        FILE15 12-OCT-1983 07:48   LPA0:  12-OCT-1983 07:51   DISK$I
/VMS   PARKIN        FILE15 12-OCT-1983 07:48   LPA0:  12-OCT-1983 07:51   DISK$I
/VMS   PARKIN        FILE15 12-OCT-1983 07:48   LPA0:  12-OCT-1983 07:51   DISK$I
```

Probability (per 10^5) of death (upper block) and hysterectomy (lower block) at individual years of age - 3 decades.

1523	106	67	52	41	34	30	28	26	24
23	22	21	22	25	25	35	39	43	45
45	45	44	44	44	45	47	49	52	56
60	65	70	77	84	93	103	114	128	143
160	180	202	226	253	281	311	343	377	412
449	489	531	576	624	676	733	795	864	941
1025	1120	1227	1348	1486	1641	1818	2017	2243	2498
2784	3104	3462	3860	4301	4787	5323	5910	6550	7250
8014	8846	9752	10734	11795	12937	14157	15456	16831	18281
19805	21413	23113	24912	26817	31714	34049	36505	39075	99999
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	20	40	80	120	160
220	260	300	380	460	540	620	680	740	800
860	900	900	800	700	600	520	460	400	340
280	220	160	156	152	148	144	140	144	148
152	156	160	156	152	148	144	140	132	124
116	108	100	98	96	94	92	90	88	86
84	82	80	80	80	80	80	80	80	80
80	80	80	80	80	80	80	80	80	80
1523	106	67	52	41	34	30	28	26	24
23	22	21	22	25	25	35	39	43	45
45	45	44	44	44	45	47	49	52	56
60	65	70	77	84	93	103	114	128	143
160	180	202	226	253	281	311	343	377	412
449	489	531	576	624	676	733	795	864	941
1025	1120	1227	1348	1486	1641	1818	2017	2243	2498
2784	3104	3462	3860	4301	4787	5323	5910	6550	7250
8014	8846	9752	10734	11795	12937	14157	15456	16831	18281
19805	21413	23113	24912	26817	31714	34049	36505	39075	99999
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	20	40	80	120	160
220	260	300	380	460	540	620	680	740	800
860	900	900	800	700	600	520	460	400	340
280	220	160	156	152	148	144	140	144	148
152	156	160	156	152	148	144	140	132	124
116	108	100	98	96	94	92	90	88	86
84	82	80	80	80	80	80	80	80	80
80	80	80	80	80	80	80	80	80	80
1523	106	67	52	41	34	30	28	26	24
23	22	21	22	25	25	35	39	43	45
45	45	44	44	44	45	47	49	52	56
60	65	70	77	84	93	103	114	128	143
160	180	202	226	253	281	311	343	377	412
449	489	531	576	624	676	733	795	864	941
1025	1120	1227	1348	1486	1641	1818	2017	2243	2498
2784	3104	3462	3860	4301	4787	5323	5910	6550	7250
8014	8846	9752	10734	11795	12937	14157	15456	16831	18281
19805	21413	23113	24912	26817	31714	34049	36505	39075	99999
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	20	40	80	120	160
220	260	300	380	460	540	620	680	740	800
860	900	900	800	700	600	520	460	400	340
280	220	160	156	152	148	144	140	144	148
152	156	160	156	152	148	144	140	132	124
116	108	100	98	96	94	92	90	88	86
84	82	80	80	80	80	80	80	80	80
80	80	80	80	80	80	80	80	80	80

```
VAX/VMS  PARKIN        FILE33  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:02    L
VAX/VMS  PARKIN        FILE33  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:02    L
VAX/VMS  PARKIN        FILE33  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:02    L
```

```
PPPP     AAA   RRRR   K   K   III   N   N
P   P   A   A  R   R  K   K   I    N   N
P   P   A   A  R   R  K  K    I    NN  N
PPPP    A   A  RRRR   KKK     I    N N N
P       AAAAA  R R    K  K    I    N  NN
P       A   A  R  R   K   K   I    N   N
P       A   A  R   R  K   K  III   N   N
```

```
FFFFFFFFFF    IIIIII    LL          EEEEEEEEEE    333333      333333
FFFFFFFFFF    IIIIII    LL          EEEEEEEEEE    333333      333333
FF              II      LL          EE          33      33  33      33
FF              II      LL          EE          33      33  33      33
FF              II      LL          EE                  33          33
FF              II      LL          EE                  33          33
FFFFFFFF        II      LL          EEEEEEEE          33          33
FFFFFFFF        II      LL          EEEEEEEE          33          33
FF              II      LL          EE                  33          33
FF              II      LL          EE                  33          33
FF              II      LL          EE          33      33  33      33
FF              II      LL          EE          33      33  33      33
FF            IIIIII    LLLLLLLLLL  EEEEEEEEEE    333333      333333
FF            IIIIII    LLLLLLLLLL  EEEEEEEEEE    333333      333333
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;      666666
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;      666666
DD      DD   AA    AA      TT          ;;;;    66
DD      DD   AA    AA      TT          ;;;;    66
DD      DD   AA    AA      TT                  66
DD      DD   AA    AA      TT                  66
DD      DD   AA    AA      TT          ;;;;    66666666
DD      DD   AA    AA      TT          ;;;;    66666666
DD      DD   AAAAAAAAAA    TT          ;;;;    66      66
DD      DD   AAAAAAAAAA    TT          ;;;;    66      66
DD      DD   AA    AA      TT            ;;    66      66
DD      DD   AA    AA      TT            ;;    66      66
DDDDDDDD     AA    AA      TT          ;;        666666
DDDDDDDD     AA    AA      TT          ;;        666666
```

```
PPPP     AAA   RRRR   K   K   III   N   N
P   P   A   A  R   R  K   K   I    N   N
P   P   A   A  R   R  K  K    I    NN  N
PPPP    A   A  RRRR   KKK     I    N N N
P       AAAAA  R R    K  K    I    N  NN
P       A   A  R  R   K   K   I    N   N
P       A   A  R   R  K   K  III   N   N
```

```
VAX/VMS  PARKIN        FILE33  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:02    L
VAX/VMS  PARKIN        FILE33  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:02    L
VAX/VMS  PARKIN        FILE33  8-FEB-1984 08:01    LPA0:   8-FEB-1984 08:02    L
```

```
0, YEAR
2, NO.  OF VARIABLES
4, 4, VAR NO.   &    NO. OF CLASSES
2, 2,  }
3, 3,  } BOUNDS
4, 4,  }
5, 5,  }
1, 15, VAR.  NO.  AND NO.  OF CLASSES FOR THIS VAR.
1, 15, BOUNDS FOR CLASS 1
16, 20,   "     "     "   2
21, 25,
26, 30,
31, 35,
36, 40,
41, 45,
46, 50,
51, 55,
56, 60,
61, 65,
66, 70,
71, 75,
76, 80,
81, 100,
0, YEAR
2, NO.  OF VARIABLES
4, 1, VAR NO.   &    NO. OF CLASSES
1, 7,  } BOUNDS
1, 15, VAR.  NO.  AND NO.  OF CLASSES FOR THIS VAR.
1, 15, BOUNDS FOR CLASS 1
16, 20,   "     "     "   2
21, 25,
26, 30,
31, 35,
36, 40,
41, 45,
46, 50,
51, 55,
56, 60,
61, 65,
66, 70,
71, 75,
76, 80,
81, 100,
5, YEAR
2, NO.  OF VARIABLES
4, 4, VAR NO.   &    NO. OF CLASSES
2, 2,  }
3, 3,  } BOUNDS
4, 4,  }
5, 5,  }
1, 15, VAR.  NO.  AND NO.  OF CLASSES FOR THIS VAR.
1, 15, BOUNDS FOR CLASS 1
16, 20,   "     "     "   2
21, 25,
26, 30,
31, 35,
36, 40,
41, 45,
46, 50,
51, 55,
56, 60,
```

```
61,65,
66,70,
71,75,
76,80,
81,100,
5,YEAR
2,NO. OF VARIABLES
4,1,VAR NO.   &   NO.OF CLASSES
1,7,  } BOUNDS
1,15,VAR. NO. AND NO. OF CLASSES FOR THIS VAR.
1,15,BOUNDS FOR CLASS 1
16,20,   "    "    "   2
21,25,
26,30,
31,35,
36,40,
41,45,
46,50,
51,55,
56,60,
61,65,
66,70,
71,75,
76,80,
81,100,
15,YEAR
2,NO. OF VARIABLES
4,4,VAR NO.   &   NO.OF CLASSES
2,2,  }
3,3,  } BOUNDS
4,4,  }
5,5,  }
1,15,VAR. NO. AND NO. OF CLASSES FOR THIS VAR.
1,15,BOUNDS FOR CLASS 1
16,20,   "    "    "   2
21,25,
26,30,
31,35,
36,40,
41,45,
46,50,
51,55,
56,60,
61,65,
66,70,
71,75,
76,80,
81,100,
15,YEAR
2,NO. OF VARIABLES
4,1,VAR NO.   &   NO.OF CLASSES
1,7,  } BOUNDS
1,15,VAR. NO. AND NO. OF CLASSES FOR THIS VAR.
1,15,BOUNDS FOR CLASS 1
16,20,   "    "    "   2
21,25,
26,30,
31,35,
36,40,
41,45,
46,50,
```

```
51,55,
56,60,
61,65,
66,70,
71,75,
76,80,
81,100,
25,YEAR
2,NO. OF VARIABLES
4,4,VAR NO.   &   NO.OF CLASSES
2,2, }
3,3, } BOUNDS
4,4, }
5,5, }
1,15,VAR. NO. AND NO. OF CLASSES FOR THIS VAR.
1,15,BOUNDS FOR CLASS 1
16,20,  "    "    "   2
21,25,
26,30,
31,35,
36,40,
41,45,
46,50,
51,55,
56,60,
61,65,
66,70,
71,75,
76,80,
81,100,
25,YEAR
2,NO. OF VARIABLES
4,1,VAR NO.   &   NO.OF CLASSES
1,7, } BOUNDS
1,15,VAR. NO. AND NO. OF CLASSES FOR THIS VAR.
1,15,BOUNDS FOR CLASS 1
16,20,  "    "    "   2
21,25,
26,30,
31,35,
36,40,
41,45,
46,50,
51,55,
56,60,
61,65,
66,70,
71,75,
76,80,
81,100,
```

```
AX/VMS  PARKIN        FILE92  6-DEC-1983 08:55   LPA0:   6-DEC-1983 08:55   US:[DM
AX/VMS  PARKIN        FILE92  6-DEC-1983 08:55   LPA0:   6-DEC-1983 08:55   US:[DM
AX/VMS  PARKIN        FILE92  6-DEC-1983 08:55   LPA0:   6-DEC-1983 08:55   US:[DM
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K    III    N   N
```

```
FFFFFFFFFF     IIIIII     LL           EEEEEEEEEE     999999       222222
FFFFFFFFFF     IIIIII     LL           EEEEEEEEEE     999999       222222
FF               II       LL           EE           99      99   22      22
FF               II       LL           EE           99      99   22      22
FF               II       LL           EE           99      99           22
FF               II       LL           EE           99      99           22
FFFFFFFF         II       LL           EEEEEEEE       99999999         22
FFFFFFFF         II       LL           EEEEEEEE       99999999         22
FF               II       LL           EE                   99     22
FF               II       LL           EE                   99     22
FF               II       LL           EE                   99   22
FF               II       LL           EE                   99   22
FF             IIIIII     LLLLLLLLLL   EEEEEEEEEE     999999     2222222222
FF             IIIIII     LLLLLLLLLL   EEEEEEEEEE     999999     2222222222
```

```
DDDDDDDD       AAAAAA     TTTTTTTTTT       ;;;;       222222
DDDDDDDD       AAAAAA     TTTTTTTTTT       ;;;;       222222
DD       DD   AA    AA       TT           ;;;;     22      22
DD       DD   AA    AA       TT           ;;;;     22      22
DD       DD   AA    AA       TT                            22
DD       DD   AA    AA       TT                            22
DD       DD   AA    AA       TT           ;;;;          22
DD       DD   AA    AA       TT           ;;;;          22
DD       DD   AAAAAAAAAA     TT           ;;;;        22
DD       DD   AAAAAAAAAA     TT           ;;;;        22
DD       DD   AA    AA       TT             ;;      22
DD       DD   AA    AA       TT             ;;      22
DDDDDDDD      AA    AA       TT           ;;      2222222222
DDDDDDDD      AA    AA       TT           ;;      2222222222
```

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K    III    N   N
```

```
-X/VMS  PARKIN        FILE92  6-DEC-1983 08:55   LPA0:   6-DEC-1983 08:55   US:[DM
-X/VMS  PARKIN        FILE92  6-DEC-1983 08:55   LPA0:   6-DEC-1983 08:55   US:[DM
-X/VMS  PARKIN        FILE92  6-DEC-1983 08:55   LPA0:   6-DEC-1983 08:55   US:[DM
```

```
15100100100
```

```
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
36 52 69 80 86 91 94 96 97 98 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
37 54 68 79 86 91 94 96 97 98 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
38 55 70 79 86 91 94 96 97 98 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
39 55 70 80 86 91 94 96 97 98 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
40 53 69 80 86 91 94 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
41 51 68 79 86 91 94 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
42 53 68 79 86 91 94 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
43 54 69 79 86 91 94 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
44 55 70 80 86 91 94 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
45 52 68 79 86 90 94 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 6 50 67 78 85 90 93 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 7 52 66 78 85 90 93 95 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
-8 53 68 77 85 90 93 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 9 54 69 79 85 90 93 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
-0 46 64 76 83 88 92 95 97 98 98 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 1 36 57 71 81 87 91 94 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
-2 36 50 66 77 85 90 93 95 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 3 37 50 60 74 82 88 92 94 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
-4 37 50 61 69 79 86 91 94 95 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001
  1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
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                    P   P   A   A   R   R   K  K      I     NN  N
                    PPPP    A   A   RRRR    KKK       I     N N N
                    P       AAAAA   R R     K  K      I     N  NN
                    P       A   A   R  R    K   K     I     N   N
                    P       A   A   R   R   K   K    III    N   N

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  FF               II       LL          EE           99      99  33       33
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  FF               II       LL          EE                   99  33       33
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                    PPPP    A   A   RRRR    KKK       I     N N N
                    P       AAAAA   R R     K  K      I     N  NN
                    P       A   A   R  R    K   K     I     N   N
                    P       A   A   R   R   K   K    III    N   N

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.X/VMS  PARKIN        FILE93  6-DEC-1983 08:55    LPA0:   6-DEC-1983 08:56    US:[DM
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 1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
51 16 23 30 37 45 51 58 64 70 75 80 84 88 91 94 95 97 98 98 99 991001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
52 17 24 31 38 45 52 59 65 71 76 81 85 89 92 94 96 97 98 98 99 991001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
53 17 25 33 40 46 53 60 66 72 77 82 86 90 93 95 96 97 98 98 99 991001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
54 17 25 34 41 47 54 60 67 73 78 83 87 90 93 95 96 97 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
55 17 25 34 42 48 55 61 67 73 78 83 87 90 93 95 97 98 98 99 99 991001001001001001001001001001001001001001001001001001001001001001001001001001001001001
 1001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001001
```

```
 100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
56 17 26 34 42 49 56 62 68 74 79 84 88 91 94 96 97 98 98 99 99 99100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
57 17 26 34 42 49 57 63 69 74 79 84 88 91 94 96 97 98 99 99 99 99100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
58 17 26 34 42 49 57 63 69 75 80 84 88 91 94 96 97 98 99 99 99 99100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
59 17 26 34 42 49 57 63 70 75 80 85 88 92 94 96 97 98 99 99 99100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
60 18 26 34 42 49 57 63 70 76 81 85 89 92 94 96 97 98 99 99 99100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
-61 18 26 34 42 49 57 63 70 76 81 85 89 92 95 96 98 98 99 99 99100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
-62 18 26 34 42 50 57 63 70 76 81 86 89 92 95 96 98 98 99 99 99100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
-63 18 26 34 42 50 57 63 70 76 81 86 90 92 95 97 98 98 99 99 99100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
-64 18 26 34 42 50 57 64 70 76 81 85 89 93 95 97 98 98 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
-65 18 26 35 42 50 57 64 70 76 81 85 89 92 95 97 98 98 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
-66 18 26 35 43 50 57 64 70 76 81 85 89 92 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
-67 18 27 35 43 50 57 64 70 76 81 85 89 92 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
-68 18 27 35 43 50 57 64 70 76 81 86 89 92 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
-69 18 27 35 43 50 58 64 70 76 81 86 89 92 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
'0 18 27 35 43 51 58 64 71 76 81 86 89 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
'1 18 27 35 43 51 58 64 71 76 81 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
'2 18 27 35 43 51 58 64 71 76 81 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
 3 18 27 35 43 51 58 65 71 76 81 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
 4 18 27 35 43 51 58 65 71 76 81 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
 5 18 27 35 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100100100100100
```

```
76 18 27 35 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
77 18 27 35 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
78 18 27 35 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
79 18 27 35 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
80 18 27 35 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
81 18 27 35 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
82 18 27 35 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
83 18 27 35 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
84 18 27 36 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
85 18 27 36 43 51 58 65 71 77 82 86 90 93 95 97 98 99 99 99100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
  100100100100100100100100100100100100100100100100100100100100100100100100100100
```

APPENDIX 6

OUTPUT FILES

LOG FILE

FOR 034

FOR 008

FOR 009

FOR 010

```
VAX/VMS  SCRATCH       R20 13-OCT-1983 08:26   LPA0:  13-OCT-1983 08:30   DI
VAX/VMS  SCRATCH       R20 13-OCT-1983 08:26   LPA0:  13-OCT-1983 08:30   DI
VAX/VMS  SCRATCH       R20 13-OCT-1983 08:26   LPA0:  13-OCT-1983 08:30   DI
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
RRRRRRRR      222222      000000
RRRRRRRR      222222      000000
RR      RR  22      22  00      00
RR      RR  22      22  00      00
RR      RR          22  00      00
RR      RR          22  00      00
RRRRRRRR        22      00  00  00
RRRRRRRR        22      00  00  00
RR  RR        22        0000    00
RR  RR        22        0000    00
RR    RR      22        00      00      ....
RR    RR      22        00      00      ....
RR      RR  2222222222    000000        ....
RR      RR  2222222222    000000        ....
```

```
LL            000000      GGGGGGGG      ;;;;      222222
LL            000000      GGGGGGGG      ;;;;      222222
LL          00      00  GG              ;;;;    22      22
LL          00      00  GG              ;;;;    22      22
LL          00      00  GG                              22
LL          00      00  GG                              22
LL          00      00  GG              ;;;;          22
LL          00      00  GG              ;;;;          22
LL          00      00  GG  GGGGGG      ;;;;        22
LL          00      00  GG  GGGGGG      ;;;;        22
LL          00      00  GG      GG        ;;      22
LL          00      00  GG      GG        ;;      22
LLLLLLLLLL    000000      GGGGGG        ;;      2222222222
LLLLLLLLLL    000000      GGGGGG        ;;      2222222222
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
VAX/VMS  SCRATCH       R20 13-OCT-1983 08:26   LPA0:  13-OCT-1983 08:30   DI
VAX/VMS  SCRATCH       R20 13-OCT-1983 08:26   LPA0:  13-OCT-1983 08:30   DI
VAX/VMS  SCRATCH       R20 13-OCT-1983 08:26   LPA0:  13-OCT-1983 08:30   DI
```

```
$ SET NOVER

#6     WEDNESDAY ,  12-OCT-1983 09:18:45
```

THE I.A.R.C. CERVICAL CYTOLOGY SCREENING MODEL

Y E A R 0

```
NUMBER IN STATE  1 ...      96333
NUMBER IN STATE  2 ...        675
NUMBER IN STATE  3 ...        425
NUMBER IN STATE  4 ...         45
NUMBER IN STATE  5 ...         98
NUMBER IN STATE  6 ...          0
NUMBER IN STATE  7 ...       2424
NUMBER IN STATE  8 ...          0
NUMBER IN STATE  9 ...          0

TOTAL POPULATION .....     100000
```

Y E A R 1

FROM STATE	T O S T A T E 1	2	3	4	5	6	7	8	9
1	95026	214	3	0	0	24	186	0	880
2	152	457	21	0	0	36	1	0	8
3	2	3	369	26	0	19	3	0	3
4	0	0	0	18	23	4	0	0	0
5	0	0	0	0	87	0	1	9	1
6	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	2359	0	65
8	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0

```
TOTAL SCREENED THIS YEAR      4153( 46% ELLIGIBLE)
TOTAL SCREENED TO DATE        4153( 46% ELLIGIBLE)
                                 1     2     3     4     5
TOTAL POSITIVE TESTS TO DATE    24    36    19     4     0


NUMBER IN STATE  1 ...      96853
NUMBER IN STATE  2 ...        674
NUMBER IN STATE  3 ...        393
NUMBER IN STATE  4 ...         44
NUMBER IN STATE  5 ...        110
NUMBER IN STATE  6 ...         83
NUMBER IN STATE  7 ...       2550
NUMBER IN STATE  8 ...          9
NUMBER IN STATE  9 ...        957
```

TOTAL POPULATION 100707

NUMBER OF BIRTHS 1673

YEAR 2

FROM STATE	TO STATE								
	1	2	3	4	5	6	7	8	9
1	95500	227	4	0	0	16	177	0	929
2	148	456	25	0	0	40	0	0	5
3	0	3	341	27	0	17	1	0	4
4	0	0	0	16	21	4	2	0	1
5	0	0	0	0	100	0	2	5	3
6	25	3	3	0	0	50	1	0	1
7	0	0	0	0	0	0	2487	0	63
8	0	0	0	0	0	0	0	9	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3907(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 8060(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	40	76	36	8	0

NUMBER IN STATE 1 ... 97370
NUMBER IN STATE 2 ... 689
NUMBER IN STATE 3 ... 373
NUMBER IN STATE 4 ... 43
NUMBER IN STATE 5 ... 121
NUMBER IN STATE 6 ... 127
NUMBER IN STATE 7 ... 2670
NUMBER IN STATE 8 ... 14
NUMBER IN STATE 9 ... 1006

TOTAL POPULATION 101393

NUMBER OF BIRTHS 1697

YEAR 3

FROM STATE	TO STATE								
	1	2	3	4	5	6	7	8	9
1	96013	198	4	0	0	22	170	0	963
2	137	500	21	0	0	22	1	0	8
3	0	1	326	25	0	19	0	0	2
4	0	0	0	19	20	4	0	0	0
5	0	0	0	0	106	0	1	12	2
6	14	3	1	0	0	106	0	0	3
7	0	0	0	0	0	0	2609	0	61
8	0	0	0	0	0	0	0	14	0

9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3708(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 11768(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	62	98	55	12	0

NUMBER IN STATE 1 ...	97754
NUMBER IN STATE 2 ...	702
NUMBER IN STATE 3 ...	352
NUMBER IN STATE 4 ...	44
NUMBER IN STATE 5 ...	126
NUMBER IN STATE 6 ...	173
NUMBER IN STATE 7 ...	2781
NUMBER IN STATE 8 ...	26
NUMBER IN STATE 9 ...	1039
TOTAL POPULATION	101932
NUMBER OF BIRTHS	1590

Y E A R 4

FROM STATE	T O S T A T E								
	1	2	3	4	5	6	7	8	9
1	96313	218	6	0	0	27	183	0	1007
2	156	481	26	1	0	27	4	0	7
3	1	1	306	17	0	21	1	0	5
4	0	0	0	21	20	2	0	0	1
5	0	0	0	0	115	0	1	9	1
6	23	2	2	0	0	146	0	0	0
7	0	0	0	0	0	0	2717	0	64
8	0	0	0	0	0	0	0	26	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3801(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 15569(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	89	125	76	14	0

NUMBER IN STATE 1 ...	98111
NUMBER IN STATE 2 ...	702
NUMBER IN STATE 3 ...	340
NUMBER IN STATE 4 ...	39
NUMBER IN STATE 5 ...	135
NUMBER IN STATE 6 ...	223
NUMBER IN STATE 7 ...	2906
NUMBER IN STATE 8 ...	35
NUMBER IN STATE 9 ...	1085
TOTAL POPULATION	102456
NUMBER OF BIRTHS	1618

YEAR 5

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9
1	96718	258	6	0	0	15	174	0	940
2	138	497	28	1	0	31	1	0	6
3	0	4	294	12	0	23	0	0	7
4	0	0	0	13	24	2	0	0	0
5	0	0	0	0	123	0	0	11	1
6	27	6	2	0	0	186	2	0	0
7	0	0	0	0	0	0	2850	0	56
8	0	0	0	0	0	0	0	35	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3844(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 19413(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	104	156	99	16	0

NUMBER IN STATE 1 ... 98538
NUMBER IN STATE 2 ... 765
NUMBER IN STATE 3 ... 330
NUMBER IN STATE 4 ... 26
NUMBER IN STATE 5 ... 147
NUMBER IN STATE 6 ... 257
NUMBER IN STATE 7 ... 3027
NUMBER IN STATE 8 ... 46
NUMBER IN STATE 9 ... 1010

TOTAL POPULATION 103090

NUMBER OF BIRTHS 1655

YEAR 6

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9
1	97102	232	6	0	0	28	166	0	1004
2	175	523	33	0	0	27	2	0	5
3	0	1	289	20	0	16	0	0	4
4	0	0	0	12	14	0	0	0	0
5	0	0	0	0	132	0	0	13	2
6	15	6	2	0	0	230	3	0	1
7	0	0	0	0	0	0	2970	0	57
8	0	0	0	0	0	0	0	46	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3946(44% ELLIGIBLE)
TOTAL SCREENED TO DATE 23359(45% ELLIGIBLE)

	1	2	3	4	5

TOTAL POSITIVE TESTS TO DATE 132 183 115 16 0

NUMBER IN STATE 1 ... 98892
NUMBER IN STATE 2 ... 762
NUMBER IN STATE 3 ... 330
NUMBER IN STATE 4 ... 32
NUMBER IN STATE 5 ... 146
NUMBER IN STATE 6 ... 301
NUMBER IN STATE 7 ... 3141
NUMBER IN STATE 8 ... 59
NUMBER IN STATE 9 ... 1073

TOTAL POPULATION 103604

NUMBER OF BIRTHS 1600

Y E A R 7

FROM STATE	T O S T A T E 1	2	3	4	5	6	7	8	9
1	97418	232	2	0	0	17	203	0	1020
2	153	528	35	3	0	31	3	0	9
3	0	2	287	13	0	20	1	0	7
4	0	0	0	20	12	0	0	0	0
5	0	0	0	0	134	0	0	10	2
6	28	6	3	0	0	258	2	0	4
7	0	0	0	0	0	0	3074	0	67
8	0	0	0	0	0	0	0	59	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3913(46% ELLIGIBLE)
TOTAL SCREENED TO DATE 27272(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	149	214	135	16	0

NUMBER IN STATE 1 ... 99301
NUMBER IN STATE 2 ... 768
NUMBER IN STATE 3 ... 327
NUMBER IN STATE 4 ... 36
NUMBER IN STATE 5 ... 146
NUMBER IN STATE 6 ... 326
NUMBER IN STATE 7 ... 3283
NUMBER IN STATE 8 ... 69
NUMBER IN STATE 9 ... 1109

TOTAL POPULATION 104187

NUMBER OF BIRTHS 1702

Y E A R 8

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9
1	97822	239	4	1	0	16	178	0	1041
2	154	540	34	1	0	32	1	0	6
3	0	2	289	13	0	18	1	0	4
4	0	0	0	15	20	0	0	0	1
5	0	0	0	0	135	0	0	9	2
6	17	3	2	1	0	300	2	0	1
7	0	0	0	0	0	0	3212	0	71
8	0	0	0	0	0	0	0	69	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3665(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 30937(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	165	246	153	16	0

NUMBER IN STATE 1 ... 99651
NUMBER IN STATE 2 ... 784
NUMBER IN STATE 3 ... 329
NUMBER IN STATE 4 ... 31
NUMBER IN STATE 5 ... 155
NUMBER IN STATE 6 ... 366
NUMBER IN STATE 7 ... 3394
NUMBER IN STATE 8 ... 78
NUMBER IN STATE 9 ... 1126

TOTAL POPULATION 104710

NUMBER OF BIRTHS 1658

YEAR 9

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9
1	98126	243	8	0	0	18	190	0	1066
2	161	540	38	0	0	29	3	0	13
3	0	3	289	20	0	13	1	0	3
4	0	0	0	12	16	3	0	0	0
5	0	0	0	0	139	0	0	14	2
6	16	3	1	0	0	342	2	0	2
7	0	0	0	0	0	0	3327	0	67
8	0	0	0	0	0	0	0	78	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3581(44% ELLIGIBLE)
TOTAL SCREENED TO DATE 34518(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	183	275	166	19	0

NUMBER IN STATE 1 ... 100029
NUMBER IN STATE 2 ... 789

NUMBER IN STATE 3 ... 336
NUMBER IN STATE 4 ... 32
NUMBER IN STATE 5 ... 155
NUMBER IN STATE 6 ... 405
NUMBER IN STATE 7 ... 3523
NUMBER IN STATE 8 ... 92
NUMBER IN STATE 9 ... 1153

TOTAL POPULATION 105269

NUMBER OF BIRTHS 1726

YEAR 10

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9
1	98587	224	12	0	0	9	153	0	1044
2	169	550	31	0	0	27	1	0	11
3	0	3	298	17	0	15	2	0	1
4	0	0	0	16	14	2	0	0	0
5	0	0	0	0	147	0	0	6	2
6	19	3	3	0	0	374	4	0	2
7	0	0	0	0	0	0	3441	0	82
8	0	0	0	0	0	0	0	92	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3688(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 38206(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	192	302	181	21	0

NUMBER IN STATE 1 ... 100468
NUMBER IN STATE 2 ... 780
NUMBER IN STATE 3 ... 344
NUMBER IN STATE 4 ... 33
NUMBER IN STATE 5 ... 161
NUMBER IN STATE 6 ... 427
NUMBER IN STATE 7 ... 3601
NUMBER IN STATE 8 ... 98
NUMBER IN STATE 9 ... 1142

TOTAL POPULATION 105814

NUMBER OF BIRTHS 1693

YEAR 11

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9
1	98840	218	4	0	0	19	243	0	1144

2	138	573	31	2	0	22	3	0	11
3	1	2	293	17	0	22	2	0	7
4	0	0	0	12	18	1	0	0	2
5	0	0	0	0	151	0	0	7	3
6	10	5	1	0	0	402	4	0	5
7	0	0	0	0	0	0	3532	0	69
8	0	0	0	0	0	0	0	98	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3909(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 42115(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	211	324	203	22	0

NUMBER IN STATE 1 ... 100226
NUMBER IN STATE 2 ... 798
NUMBER IN STATE 3 ... 329
NUMBER IN STATE 4 ... 31
NUMBER IN STATE 5 ... 169
NUMBER IN STATE 6 ... 466
NUMBER IN STATE 7 ... 3784
NUMBER IN STATE 8 ... 105
NUMBER IN STATE 9 ... 1241

TOTAL POPULATION 105803

NUMBER OF BIRTHS 1237

Y E A R 12

FROM STATE	T O S T A T E								
	1	2	3	4	5	6	7	8	9
1	98577	226	9	0	0	20	221	0	1173
2	196	537	26	1	0	31	3	0	4
3	0	1	286	17	0	19	2	0	4
4	0	0	0	16	14	0	0	0	1
5	0	0	0	0	152	0	0	16	1
6	18	4	2	0	0	436	2	0	4
7	0	0	0	0	0	0	3693	0	91
8	0	0	0	0	0	0	0	105	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3744(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 45859(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	231	355	222	22	0

NUMBER IN STATE 1 ... 99950
NUMBER IN STATE 2 ... 768
NUMBER IN STATE 3 ... 323
NUMBER IN STATE 4 ... 34
NUMBER IN STATE 5 ... 166
NUMBER IN STATE 6 ... 506
NUMBER IN STATE 7 ... 3921

NUMBER IN STATE 8 ... 121
NUMBER IN STATE 9 ... 1278

TOTAL POPULATION 105668

NUMBER OF BIRTHS 1159

YEAR 13

FROM STATE	TO STATE								
	1	2	3	4	5	6	7	8	9
1	98393	230	7	0	0	19	211	0	1090
2	142	559	30	0	0	26	2	0	9
3	1	4	279	14	0	19	0	0	6
4	0	0	0	16	16	1	0	0	1
5	0	0	0	0	153	0	1	7	5
6	20	5	3	0	0	471	3	0	4
7	0	0	0	0	0	0	3838	0	83
8	0	0	0	0	0	0	0	121	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3481(44% ELLIGIBLE)
TOTAL SCREENED TO DATE 49340(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	250	381	241	23	0

NUMBER IN STATE 1 ... 99741
NUMBER IN STATE 2 ... 798
NUMBER IN STATE 3 ... 319
NUMBER IN STATE 4 ... 30
NUMBER IN STATE 5 ... 169
NUMBER IN STATE 6 ... 536
NUMBER IN STATE 7 ... 4055
NUMBER IN STATE 8 ... 128
NUMBER IN STATE 9 ... 1198

TOTAL POPULATION 105648

NUMBER OF BIRTHS 1185

YEAR 14

FROM STATE	TO STATE								
	1	2	3	4	5	6	7	8	9
1	98125	238	7	0	0	24	228	0	1119
2	178	552	26	1	0	31	1	0	9
3	0	3	275	18	0	18	3	0	2
4	0	0	0	9	17	4	0	0	0
5	0	0	0	0	159	0	0	6	4
6	21	4	0	0	0	501	6	0	4

7	0	0	0	0	0	0	3978	0	77
8	0	0	0	0	0	0	0	128	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3502(44% ELLIGIBLE)
TOTAL SCREENED TO DATE 52842(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	274	412	259	27	0

NUMBER IN STATE 1 ... 99529
NUMBER IN STATE 2 ... 797
NUMBER IN STATE 3 ... 308
NUMBER IN STATE 4 ... 28
NUMBER IN STATE 5 ... 176
NUMBER IN STATE 6 ... 578
NUMBER IN STATE 7 ... 4216
NUMBER IN STATE 8 ... 134
NUMBER IN STATE 9 ... 1215

TOTAL POPULATION 105632

NUMBER OF BIRTHS 1205

Y E A R 15

FROM STATE	T O S T A T E								
	1	2	3	4	5	6	7	8	9
1	97971	254	4	0	0	15	176	0	1109
2	148	568	29	3	0	36	1	0	12
3	1	1	275	14	0	15	0	0	2
4	0	0	0	13	12	2	0	0	1
5	0	0	0	0	163	0	0	10	3
6	22	6	3	0	0	537	6	0	4
7	0	0	0	0	0	0	4115	0	101
8	0	0	0	0	0	0	0	134	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3511(44% ELLIGIBLE)
TOTAL SCREENED TO DATE 56353(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	289	448	274	29	0

NUMBER IN STATE 1 ... 99317
NUMBER IN STATE 2 ... 829
NUMBER IN STATE 3 ... 311
NUMBER IN STATE 4 ... 30
NUMBER IN STATE 5 ... 175
NUMBER IN STATE 6 ... 605
NUMBER IN STATE 7 ... 4298
NUMBER IN STATE 8 ... 144
NUMBER IN STATE 9 ... 1232

TOTAL POPULATION 105565

NUMBER OF BIRTHS 1175

Y E A R 16

FROM STATE	T O S T A T E								
	1	2	3	4	5	6	7	8	9
1	97690	228	1	0	0	18	215	0	1165
2	171	583	36	3	0	24	6	0	6
3	0	2	278	11	0	15	1	0	4
4	0	0	0	11	15	2	0	0	2
5	0	0	0	0	161	0	0	10	4
6	15	7	2	0	0	572	4	0	5
7	0	0	0	0	0	0	4204	0	94
8	0	0	0	0	0	0	0	144	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3632(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 59985(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	307	472	289	31	0

NUMBER IN STATE 1 ... 99060
NUMBER IN STATE 2 ... 820
NUMBER IN STATE 3 ... 317
NUMBER IN STATE 4 ... 25
NUMBER IN STATE 5 ... 176
NUMBER IN STATE 6 ... 631
NUMBER IN STATE 7 ... 4430
NUMBER IN STATE 8 ... 154
NUMBER IN STATE 9 ... 1280

TOTAL POPULATION 105459

NUMBER OF BIRTHS 1184

Y E A R 17

FROM STATE	T O S T A T E								
	1	2	3	4	5	6	7	8	9
1	97431	230	8	0	0	14	207	0	1170
2	150	586	35	0	0	33	2	0	14
3	0	2	277	18	0	16	0	0	4
4	0	0	0	8	14	3	0	0	0
5	0	0	0	0	158	0	0	11	7
6	20	3	4	0	0	598	1	0	5
7	0	0	0	0	0	0	4339	0	91
8	0	0	0	0	0	0	0	154	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3574(45% ELLIGIBLE)

TOTAL SCREENED TO DATE 63559(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	321	505	305	34	0

NUMBER IN STATE 1 ...	98820
NUMBER IN STATE 2 ...	821
NUMBER IN STATE 3 ...	324
NUMBER IN STATE 4 ...	26
NUMBER IN STATE 5 ...	172
NUMBER IN STATE 6 ...	664
NUMBER IN STATE 7 ...	4549
NUMBER IN STATE 8 ...	165
NUMBER IN STATE 9 ...	1291
TOTAL POPULATION	105376
NUMBER OF BIRTHS	1219

Y E A R 18

FROM STATE	T O S T A T E								
	1	2	3	4	5	6	7	8	9
1	97180	246	6	0	0	21	234	0	1133
2	158	590	32	1	0	31	2	0	7
3	0	4	278	16	0	19	4	0	3
4	0	0	0	13	10	1	1	0	1
5	0	0	0	0	153	0	0	10	9
6	14	4	1	0	0	635	3	0	7
7	0	0	0	0	0	0	4441	0	108
8	0	0	0	0	0	0	0	165	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3440(44% ELLIGIBLE)
TOTAL SCREENED TO DATE 66999(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	342	536	324	35	0

NUMBER IN STATE 1 ...	98531
NUMBER IN STATE 2 ...	844
NUMBER IN STATE 3 ...	317
NUMBER IN STATE 4 ...	30
NUMBER IN STATE 5 ...	163
NUMBER IN STATE 6 ...	707
NUMBER IN STATE 7 ...	4685
NUMBER IN STATE 8 ...	175
NUMBER IN STATE 9 ...	1268
TOTAL POPULATION	105277
NUMBER OF BIRTHS	1179

Y E A R 19

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9
1	96950	217	5	0	0	18	201	0	1140
2	152	619	33	1	0	31	1	0	7
3	1	6	275	14	0	18	1	0	2
4	0	0	0	15	14	0	1	0	0
5	0	0	0	0	147	0	0	11	5
6	22	3	2	0	0	671	3	0	6
7	0	0	0	0	0	0	4583	0	102
8	0	0	0	0	0	0	0	175	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3429(45% ELLIGIBLE) .
TOTAL SCREENED TO DATE 70428(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	360	567	342	35	0

NUMBER IN STATE 1 ... 98388
NUMBER IN STATE 2 ... 845
NUMBER IN STATE 3 ... 315
NUMBER IN STATE 4 ... 30
NUMBER IN STATE 5 ... 161
NUMBER IN STATE 6 ... 738
NUMBER IN STATE 7 ... 4790
NUMBER IN STATE 8 ... 186
NUMBER IN STATE 9 ... 1262

TOTAL POPULATION 105267

NUMBER OF BIRTHS 1263

Y E A R 20

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9
1	96654	278	4	0	0	18	234	0	1200
2	184	598	21	0	0	28	2	0	12
3	0	2	285	14	0	11	0	0	3
4	0	0	0	13	16	1	0	0	0
5	0	0	0	0	146	0	0	7	8
6	21	3	5	1	0	698	2	0	8
7	0	0	0	0	0	0	4671	0	119
8	0	0	0	0	0	0	0	186	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3517(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 73945(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	378	595	353	36	0

NUMBER IN STATE 1 ... 98160
NUMBER IN STATE 2 ... 881
NUMBER IN STATE 3 ... 315
NUMBER IN STATE 4 ... 28
NUMBER IN STATE 5 ... 162
NUMBER IN STATE 6 ... 756
NUMBER IN STATE 7 ... 4909
NUMBER IN STATE 8 ... 193
NUMBER IN STATE 9 ... 1350

TOTAL POPULATION 105211

NUMBER OF BIRTHS 1301

Y E A R 21

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9
1	96489	226	4	0	0	14	203	0	1224
2	181	610	39	1	0	40	2	0	8
3	0	0	275	16	0	19	1	0	4
4	0	0	0	11	14	2	0	0	1
5	0	0	0	0	146	0	1	10	5
6	21	3	1	0	0	717	3	0	11
7	0	0	0	0	0	0	4817	0	92
8	0	0	0	0	0	0	0	193	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3498(44% ELLIGIBLE)
TOTAL SCREENED TO DATE 77443(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	392	635	372	38	0

NUMBER IN STATE 1 ... 98062
NUMBER IN STATE 2 ... 839
NUMBER IN STATE 3 ... 319
NUMBER IN STATE 4 ... 28
NUMBER IN STATE 5 ... 160
NUMBER IN STATE 6 ... 792
NUMBER IN STATE 7 ... 5027
NUMBER IN STATE 8 ... 203
NUMBER IN STATE 9 ... 1345

TOTAL POPULATION 105227

NUMBER OF BIRTHS 1371

Y E A R 22

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9

1	96385	240	8	0	0	16	211	0	1202
2	180	591	25	0	0	32	2	0	9
3	0	0	271	15	0	29	1	0	3
4	0	0	0	14	12	1	0	0	1
5	0	0	0	0	147	0	2	8	3
6	15	7	2	0	0	756	5	0	7
7	0	0	0	0	0	0	4917	0	110
8	0	0	0	0	0	0	0	203	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3718(46% ELLIGIBLE)
TOTAL SCREENED TO DATE 81161(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	408	667	401	39	0

NUMBER IN STATE 1 ... 98014
NUMBER IN STATE 2 ... 838
NUMBER IN STATE 3 ... 306
NUMBER IN STATE 4 ... 29
NUMBER IN STATE 5 ... 159
NUMBER IN STATE 6 ... 834
NUMBER IN STATE 7 ... 5138
NUMBER IN STATE 8 ... 211
NUMBER IN STATE 9 ... 1335

TOTAL POPULATION 105318

NUMBER OF BIRTHS 1434

Y E A R 23

FROM STATE	T O S T A T E								
	1	2	3	4	5	6	7	8	9
1	96315	242	1	0	0	16	220	0	1220
2	173	582	27	0	0	43	3	0	10
3	0	1	265	20	0	16	1	0	3
4	0	0	0	11	14	0	0	0	4
5	0	0	0	0	145	0	1	6	7
6	18	3	3	0	0	799	5	0	6
7	0	0	0	0	0	0	5020	0	118
8	0	0	0	0	0	0	0	211	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3655(47% ELLIGIBLE)
TOTAL SCREENED TO DATE 84816(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	424	710	417	39	0

NUMBER IN STATE 1 ... 97897
NUMBER IN STATE 2 ... 828
NUMBER IN STATE 3 ... 296
NUMBER IN STATE 4 ... 31
NUMBER IN STATE 5 ... 159

NUMBER IN STATE 6 ... 874
NUMBER IN STATE 7 ... 5250
NUMBER IN STATE 8 ... 217
NUMBER IN STATE 9 ... 1368

TOTAL POPULATION 105335

NUMBER OF BIRTHS 1391

Y E A R 24

FROM STATE	T O S T A T E								
	1	2	3	4	5	6	7	8	9
1	96300	252	5	0	0	15	202	0	1123
2	176	582	28	1	0	28	2	0	11
3	0	2	258	13	0	17	2	0	4
4	0	0	0	16	13	2	0	0	0
5	0	0	0	0	145	0	0	6	8
6	17	9	2	0	0	831	1	0	14
7	0	0	0	0	0	0	5122	0	128
8	0	0	0	0	0	0	0	217	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3494(46% ELLIGIBLE)
TOTAL SCREENED TO DATE 88310(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	439	738	434	41	0

NUMBER IN STATE 1 ... 97958
NUMBER IN STATE 2 ... 845
NUMBER IN STATE 3 ... 293
NUMBER IN STATE 4 ... 30
NUMBER IN STATE 5 ... 158
NUMBER IN STATE 6 ... 893
NUMBER IN STATE 7 ... 5329
NUMBER IN STATE 8 ... 223
NUMBER IN STATE 9 ... 1288

TOTAL POPULATION 105506

NUMBER OF BIRTHS 1465

Y E A R 25

FROM STATE	T O S T A T E								
	1	2	3	4	5	6	7	8	9
1	96256	245	5	0	0	18	220	0	1214
2	182	584	33	1	0	35	3	0	7
3	0	3	259	13	0	15	1	0	2
4	0	0	0	13	16	1	0	0	0

5	0	0	0	0	143	0	1	10	4
6	19	3	2	0	0	849	3	0	17
7	0	0	0	0	0	0	5217	0	112
8	0	0	0	0	0	0	0	223	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3553(46% ELLIGIBLE)
TOTAL SCREENED TO DATE 91863(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	457	773	449	42	0

NUMBER IN STATE 1 ... 97905
NUMBER IN STATE 2 ... 835
NUMBER IN STATE 3 ... 299
NUMBER IN STATE 4 ... 27
NUMBER IN STATE 5 ... 159
NUMBER IN STATE 6 ... 918
NUMBER IN STATE 7 ... 5445
NUMBER IN STATE 8 ... 233
NUMBER IN STATE 9 ... 1356

TOTAL POPULATION 105588

NUMBER OF BIRTHS 1448

Y E A R 26

FROM STATE	T O S T A T E 1	2	3	4	5	6	7	8	9
1	96243	244	10	0	0	16	233	0	1159
2	179	580	32	0	0	33	3	0	8
3	1	0	267	19	0	11	1	0	0
4	0	0	0	13	14	0	0	0	0
5	0	0	0	0	147	0	0	9	3
6	20	8	1	0	0	873	4	0	12
7	0	0	0	0	0	0	5322	0	123
8	0	0	0	0	0	0	0	233	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3485(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 95348(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	473	806	460	42	0

NUMBER IN STATE 1 ... 97901
NUMBER IN STATE 2 ... 832
NUMBER IN STATE 3 ... 310
NUMBER IN STATE 4 ... 32
NUMBER IN STATE 5 ... 161
NUMBER IN STATE 6 ... 933
NUMBER IN STATE 7 ... 5563
NUMBER IN STATE 8 ... 242
NUMBER IN STATE 9 ... 1305

TOTAL POPULATION 105732

NUMBER OF BIRTHS 1458

Y E A R 27

FROM STATE	T O STATE								
	1	2	3	4	5	6	7	8	9
1	96143	253	7	1	0	17	214	0	1266
2	187	573	27	1	0	31	3	0	10
3	0	4	268	12	0	19	2	0	5
4	0	0	0	17	13	0	0	0	2
5	0	0	0	0	142	0	0	14	5
6	17	6	1	0	0	894	2	0	13
7	0	0	0	0	0	0	5435	0	128
8	0	0	0	0	0	0	0	242	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3592(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 98940(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	490	837	479	42	0

NUMBER IN STATE 1 ... 97783
NUMBER IN STATE 2 ... 836
NUMBER IN STATE 3 ... 303
NUMBER IN STATE 4 ... 31
NUMBER IN STATE 5 ... 155
NUMBER IN STATE 6 ... 961
NUMBER IN STATE 7 ... 5656
NUMBER IN STATE 8 ... 256
NUMBER IN STATE 9 ... 1429

TOTAL POPULATION 105725

NUMBER OF BIRTHS 1436

Y E A R 28

FROM STATE	T O STATE								
	1	2	3	4	5	6	7	8	9
1	96066	277	4	1	0	19	243	0	1173
2	192	581	25	1	0	26	1	0	10
3	1	1	277	6	0	15	0	0	3
4	0	0	0	12	18	1	0	0	0
5	0	0	0	0	142	0	0	10	3
6	20	2	3	0	0	917	3	0	16
7	0	0	0	0	0	0	5538	0	118
8	0	0	0	0	0	0	0	256	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3627(46% ELLIGIBLE)
TOTAL SCREENED TO DATE 102567(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	509	863	494	43	0

NUMBER IN STATE 1 ... 97749
NUMBER IN STATE 2 ... 861
NUMBER IN STATE 3 ... 309
NUMBER IN STATE 4 ... 20
NUMBER IN STATE 5 ... 160
NUMBER IN STATE 6 ... 978
NUMBER IN STATE 7 ... 5785
NUMBER IN STATE 8 ... 266
NUMBER IN STATE 9 ... 1323

TOTAL POPULATION 105862

NUMBER OF BIRTHS 1470

Y E A R 29

FROM STATE	T O S T A T E 1	2	3	4	5	6	7	8	9
1	96037	238	7	0	0	14	224	0	1229
2	173	602	36	1	0	42	3	0	4
3	0	2	264	13	0	19	1	0	10
4	0	0	0	6	12	0	0	0	2
5	0	0	0	0	141	0	1	15	3
6	19	3	2	0	0	933	3	0	18
7	0	0	0	0	0	0	5680	0	105
8	0	0	0	0	0	0	0	266	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3611(46% ELLIGIBLE)
TOTAL SCREENED TO DATE 106178(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	523	905	513	43	0

NUMBER IN STATE 1 ... 97726
NUMBER IN STATE 2 ... 845
NUMBER IN STATE 3 ... 309
NUMBER IN STATE 4 ... 20
NUMBER IN STATE 5 ... 153
NUMBER IN STATE 6 ... 1008
NUMBER IN STATE 7 ... 5912
NUMBER IN STATE 8 ... 281
NUMBER IN STATE 9 ... 1371

TOTAL POPULATION 105973

NUMBER OF BIRTHS 1497

Y E A R 30

FROM STATE	TO STATE 1	2	3	4	5	6	7	8	9
1	96044	252	10	0	0	13	200	0	1207
2	192	592	23	1	0	31	2	0	4
3	0	0	276	10	0	20	2	0	1
4	0	0	0	10	8	1	0	0	1
5	0	0	0	0	141	0	0	7	5
6	18	5	1	0	0	969	1	0	14
7	0	0	0	0	0	0	5759	0	153
8	0	0	0	0	0	0	0	281	0
9	0	0	0	0	0	0	0	0	0

TOTAL SCREENED THIS YEAR 3407(45% ELLIGIBLE)
TOTAL SCREENED TO DATE 109585(45% ELLIGIBLE)

	1	2	3	4	5
TOTAL POSITIVE TESTS TO DATE	536	936	533	44	0

NUMBER IN STATE 1 ... 97684
NUMBER IN STATE 2 ... 849
NUMBER IN STATE 3 ... 310
NUMBER IN STATE 4 ... 21
NUMBER IN STATE 5 ... 149
NUMBER IN STATE 6 ... 1034
NUMBER IN STATE 7 ... 5964
NUMBER IN STATE 8 ... 288
NUMBER IN STATE 9 ... 1385

TOTAL POPULATION 106011

NUMBER OF BIRTHS 1430

FORTRAN STOP
Job 42 entered on queue LPA0
FORTRAN STOP
Job 43 entered on queue LPA0
SCRATCH job terminated at 12-OCT-1983 11:31:44.88

Accounting information:

Buffered I/O count:	169	Peak working set size:	250
Direct I/O count:	831	Peak page file size:	2858
Page faults:	138196	Mounted volumes:	0
Elapsed CPU time:	0 01:48:18.17	Elapsed time:	0 02:13:01.03

```
VAX/VMS  SCRATCH      FOR034 13-OCT-1983 08:24   LPA0:  13-OCT-1983 08:24
VAX/VMS  SCRATCH      FOR034 13-OCT-1983 08:24   LPA0:  13-OCT-1983 08:24
VAX/VMS  SCRATCH      FOR034 13-OCT-1983 08:24   LPA0:  13-OCT-1983 08:24
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
FFFFFFFFFF    000000    RRRRRRRR      000000      333333    44    44
FFFFFFFFFF    000000    RRRRRRRR      000000      333333    44    44
FF           00    00   RR     RR    00    00    33    33   44    44
FF           00    00   RR     RR    00    00    33    33   44    44
FF           00    00   RR     RR    00  0000          33   44    44
FF           00    00   RR     RR    00  0000          33   44    44
FFFFFFFF     00    00   RRRRRRRR    00  00  00        33    4444444444
FFFFFFFF     00    00   RRRRRRRR    00  00  00        33    4444444444
FF           00    00   RR  RR      0000    00          33        44
FF           00    00   RR  RR      0000    00          33        44
FF           00    00   RR   RR    00      00    33    33        44
FF           00    00   RR   RR    00      00    33    33        44
FF             000000    RR     RR    000000      333333        44
FF             000000    RR     RR    000000      333333        44
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;    77777777
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;    77777777
DD      DD   AA    AA      TT            ;;;;          77
DD      DD   AA    AA      TT            ;;;;          77
DD      DD   AA    AA      TT                          77
DD      DD   AA    AA      TT                          77
DD      DD   AA    AA      TT            ;;;;        77
DD      DD   AA    AA      TT            ;;;;        77
DD      DD   AAAAAAAAAA    TT            ;;;;      77
DD      DD   AAAAAAAAAA    TT            ;;;;      77
DD      DD   AA    AA      TT              ;;    77
DD      DD   AA    AA      TT              ;;    77
DDDDDDDD     AA    AA      TT            ;;    77
DDDDDDDD     AA    AA      TT            ;;    77
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
VAX/VMS  SCRATCH      FOR034 13-OCT-1983 08:24   LPA0:  13-OCT-1983 08:24
VAX/VMS  SCRATCH      FOR034 13-OCT-1983 08:24   LPA0:  13-OCT-1983 08:24
VAX/VMS  SCRATCH      FOR034 13-OCT-1983 08:24   LPA0:  13-OCT-1983 08:24
```

(*, 1)	0	0	0	0
(*, 2)	11	3	0	0
(*, 3)	87	6	0	0
(*, 4)	145	24	1	0
(*, 5)	118	34	2	2
(*, 6)	111	52	2	6
(*, 7)	68	46	1	5
(*, 8)	57	31	4	21
(*, 9)	45	15	2	25
(*, 10)	41	13	4	16
(*, 11)	37	18	4	20
(*, 12)	22	13	5	16
(*, 13)	38	10	0	21
(*, 14)	32	11	2	10
(*, 15)	23	23	0	17

```
VAX/VMS  SCRATCH      FOR008 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:25
VAX/VMS  SCRATCH      FOR008 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:25
VAX/VMS  SCRATCH      FOR008 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:25
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
FFFFFFFFFF    000000    RRRRRRRR      000000      000000      888888
FFFFFFFFFF    000000    RRRRRRRR      000000      000000      888888
FF           00    00   RR     RR   00    00    00    00    88    88
FF           00    00   RR     RR   00    00    00    00    88    88
FF           00    00   RR     RR   00    0000  00    0000  88    88
FF           00    00   RR     RR   00    0000  00    0000  88    88
FFFFFFFF     00    00   RRRRRRRR    00  00  00  00  00  00    888888
FFFFFFFF     00    00   RRRRRRRR    00  00  00  00  00  00    888888
FF           00    00   RR  RR      0000    00  0000    00    88    88
FF           00    00   RR  RR      0000    00  0000    00    88    88
FF           00    00   RR   RR     00      00  00      00    88    88
FF           00    00   RR   RR     00      00  00      00    88    88
FF             000000   RR     RR     000000      000000      888888
FF             000000   RR     RR     000000      000000      888888
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;        11
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;        11
DD      DD   AA    AA      TT          ;;;;       1111
DD      DD   AA    AA      TT          ;;;;       1111
DD      DD   AA    AA      TT                       11
DD      DD   AA    AA      TT                       11
DD      DD   AA    AA      TT          ;;;;         11
DD      DD   AA    AA      TT          ;;;;         11
DD      DD   AAAAAAAAAA    TT          ;;;;         11
DD      DD   AAAAAAAAAA    TT          ;;;;         11
DD      DD   AA    AA      TT            ;;         11
DD      DD   AA    AA      TT            ;;         11
DDDDDDDD     AA    AA      TT          ;;        111111
DDDDDDDD     AA    AA      TT          ;;        111111
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
VAX/VMS  SCRATCH      FOR008 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:25
VAX/VMS  SCRATCH      FOR008 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:25
VAX/VMS  SCRATCH      FOR008 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:25
```

1	65	2	3	8	0	0	5
1	76	2	3	8	0	0	5
1	66	2	3	8	0	0	5
1	65	3	1	8	0	0	5
1	91	3	2	8	0	0	5
1	54	2	3	8	0	0	5
1	80	3	0	8	0	0	5
1	49	2	3	8	0	0	5
1	55	1	1	8	0	0	5
2	70	1	1	8	0	0	5
2	49	3	3	8	0	0	5
2	75	3	0	8	0	0	5
2	59	2	3	8	0	0	5
2	75	2	3	8	0	0	5
3	76	3	3	8	0	0	5
3	53	2	2	8	0	0	5
3	45	2	3	8	0	0	5
3	62	2	0	8	0	0	5
3	61	2	0	8	0	0	5
3	50	2	3	8	0	0	5
3	49	2	1	8	0	0	5
3	45	2	3	8	0	0	5
3	79	2	3	8	0	0	5
3	65	1	1	8	0	0	5
3	64	2	3	8	0	0	5
3	56	2	3	8	0	0	5
4	43	2	3	8	0	0	5
4	54	3	2	8	0	0	5
4	54	2	3	8	0	0	5
4	53	2	3	8	0	0	5
4	38	2	3	8	0	0	5
4	60	3	2	8	0	0	5
4	58	2	3	8	0	0	5
4	43	2	2	8	0	0	5
4	72	1	1	8	0	0	5
5	68	3	0	8	0	0	5
5	73	2	2	8	0	0	5
5	52	2	0	8	0	0	5
5	72	3	3	8	0	0	5
5	79	1	2	8	0	0	5
5	62	3	2	8	0	0	5
5	55	2	3	8	0	0	5
5	60	2	3	8	0	0	5
5	54	2	3	8	0	0	5
5	51	3	3	8	0	0	5
5	57	1	1	8	0	0	5
6	51	1	1	8	0	0	5
6	73	2	3	8	0	0	5
6	63	1	2	8	0	0	5
6	59	2	2	8	0	0	5
6	63	2	3	8	0	0	5
6	69	2	2	8	0	0	5
6	53	3	2	8	0	0	5
6	77	1	1	8	0	0	5
6	29	2	3	8	0	0	5
6	51	2	2	8	0	0	5
6	56	2	2	8	0	0	5
6	53	2	3	8	0	0	5
6	45	2	3	8	0	0	5
7	59	2	2	8	0	0	5
7	48	2	1	8	0	0	5

27	66	3	2	8	0	0	5
27	64	2	3	8	0	0	5
27	58	3	3	8	0	0	5
27	55	2	3	8	0	0	5
27	52	2	3	8	0	0	5
27	52	2	3	8	0	0	5
27	86	2	3	8	0	0	5
27	55	2	2	8	0	0	5
27	49	2	1	8	0	0	5
27	42	2	3	8	0	0	5
27	85	3	3	8	0	0	5
27	38	3	3	8	0	0	5
28	58	2	3	8	0	0	5
28	66	2	2	8	0	0	5
28	51	2	3	8	0	0	5
28	81	2	2	8	0	0	5
28	54	2	3	8	0	0	5
28	73	2	3	8	0	0	5
28	63	3	0	8	0	0	5
28	44	2	2	8	0	0	5
28	70	2	3	8	0	0	5
28	39	1	1	8	0	0	5
29	68	3	3	8	0	0	5
29	61	2	2	8	0	0	5
29	82	1	1	8	0	0	5
29	65	2	1	8	0	0	5
29	77	2	3	8	0	0	5
29	61	2	3	8	0	0	5
29	64	2	2	8	0	0	5
29	51	2	3	8	0	0	5
29	80	3	3	8	0	0	5
29	47	2	3	8	0	0	5
29	54	2	3	8	0	0	5
29	85	3	3	8	0	0	5
29	64	3	3	8	0	0	5
29	79	3	2	8	0	0	5
29	50	2	3	8	0	0	5
30	52	2	3	8	0	0	5
30	74	3	3	8	0	0	5
30	85	3	3	8	0	0	5
30	54	2	1	8	0	0	5
30	86	3	3	8	0	0	5
30	67	2	3	8	0	0	5
30	82	1	1	8	0	0	5

```
VAX/VMS  SCRATCH        FOR009 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:26
VAX/VMS  SCRATCH        FOR009 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:26
VAX/VMS  SCRATCH        FOR009 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:26

                 SSSS    CCCC  RRRR     AAA    TTTTT   CCCC  H   H
                S       C      R   R   A   A     T    C      H   H
                S       C      R   R   A   A     T    C      H   H
                 SSS    C      RRRR    A   A     T    C      HHHHH
                    S   C      R R     AAAAA     T    C      H   H
                    S   C      R  R    A   A     T    C      H   H
                SSSS     CCCC  R   R   A   A     T     CCCC  H   H

FFFFFFFFFF     000000    RRRRRRRR      000000      000000      999999
FFFFFFFFFF     000000    RRRRRRRR      000000      000000      999999
FF            00    00   RR     RR   00    00    00    00    99    99
FF            00    00   RR     RR   00    00    00    00    99    99
FF            00    00   RR     RR   00  0000    00  0000    99    99
FF            00    00   RR     RR   00  0000    00  0000    99    99
FFFFFFFF      00    00   RRRRRRRR    00  00  00  00  00  00    99999999
FFFFFFFF      00    00   RRRRRRRR    00  00  00  00  00  00    99999999
FF            00    00   RR   RR     0000    00  0000    00          99
FF            00    00   RR   RR     0000    00  0000    00          99
FF            00    00   RR    RR    00      00  00      00          99
FF            00    00   RR    RR    00      00  00      00          99
FF              000000     RR     RR    000000      000000      999999
FF              000000     RR     RR    000000      000000      999999

DDDDDDDD       AAAAAA     TTTTTTTTTT      ;;;;        11
DDDDDDDD       AAAAAA     TTTTTTTTTT      ;;;;        11
DD      DD    AA    AA       TT           ;;;;      1111
DD      DD    AA    AA       TT           ;;;;      1111
DD      DD    AA    AA       TT                       11
DD      DD    AA    AA       TT                       11
DD      DD    AA    AA       TT           ;;;;        11
DD      DD    AA    AA       TT           ;;;;        11
DD      DD    AAAAAAAAAA     TT           ;;;;        11
DD      DD    AAAAAAAAAA     TT           ;;;;        11
DD      DD    AA    AA       TT             ;;        11
DD      DD    AA    AA       TT             ;;        11
DDDDDDDD      AA    AA       TT           ;;        111111
DDDDDDDD      AA    AA       TT           ;;        111111

                 SSSS    CCCC  RRRR     AAA    TTTTT   CCCC  H   H
                S       C      R   R   A   A     T    C      H   H
                S       C      R   R   A   A     T    C      H   H
                 SSS    C      RRRR    A   A     T    C      HHHHH
                    S   C      R R     AAAAA     T    C      H   H
                    S   C      R  R    A   A     T    C      H   H
                SSSS     CCCC  R   R   A   A     T     CCCC  H   H

VAX/VMS  SCRATCH        FOR009 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:26
VAX/VMS  SCRATCH        FOR009 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:26
VAX/VMS  SCRATCH        FOR009 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:26
```

1	40	2	3	5	0	0	4
1	74	3	3	5	0	0	4
1	42	1	1	5	0	0	4
1	42	2	3	5	0	0	4
1	39	2	2	5	0	0	4
1	74	3	0	5	0	0	4
1	51	3	3	5	0	0	4
1	68	3	3	5	0	0	4
1	59	2	2	5	0	0	4
1	82	3	3	5	0	0	4
1	50	2	3	5	0	0	4
1	47	2	1	5	0	0	4
1	54	1	1	5	0	0	4
1	49	2	2	5	0	0	4
1	64	3	3	5	0	0	4
1	69	2	2	5	0	0	4
1	47	3	3	5	0	0	4
1	60	2	3	5	0	0	4
1	74	2	3	5	0	0	4
1	67	3	3	5	0	0	4
1	54	2	3	5	0	0	4
1	33	1	2	5	0	0	4
1	51	2	1	5	0	0	4
2	42	1	1	5	0	0	4
2	65	3	0	5	0	0	4
2	49	2	3	5	0	0	4
2	43	2	3	5	0	0	4
2	44	2	3	5	0	0	4
2	56	2	3	5	0	0	4
2	64	2	3	5	0	0	4
2	53	2	3	5	0	0	4
2	49	2	3	5	0	0	4
2	44	2	2	5	0	0	4
2	35	2	0	5	0	0	4
2	59	2	2	5	0	0	4
2	58	3	2	5	0	0	4
2	44	2	3	5	0	0	4
2	51	2	3	5	0	0	4
2	76	2	0	5	0	0	4
2	40	3	2	5	0	0	4
2	65	1	1	5	0	0	4
2	43	2	3	5	0	0	4
2	55	2	3	5	0	0	4
2	65	2	3	5	0	0	4
3	33	2	3	5	0	0	4
3	63	2	0	5	0	0	4
3	65	3	2	5	0	0	4
3	72	3	3	5	0	0	4
3	53	2	2	5	0	0	4
3	77	3	2	5	0	0	4
3	78	3	3	5	0	0	4
3	50	2	0	5	0	0	4
3	48	2	3	5	0	0	4
3	37	2	3	5	0	0	4
3	50	2	2	5	0	0	4
3	57	2	3	5	0	0	4
3	59	2	3	5	0	0	4
3	42	2	2	5	0	0	4
3	53	2	2	5	0	0	4
3	55	1	1	5	0	0	4
3	71	3	3	5	0	0	4

28	76	2	3	5	0	0	4
28	73	2	1	5	0	0	4
28	50	2	3	5	0	0	4
28	44	2	3	5	0	0	4
28	58	2	3	5	0	0	4
28	60	2	3	5	0	0	4
28	55	2	3	5	0	0	4
28	50	2	3	5	0	0	4
28	44	2	3	5	0	0	4
28	52	2	1	5	0	0	4
28	84	3	3	5	0	0	4
28	72	2	3	5	0	0	4
28	84	3	3	5	0	0	4
28	63	3	3	5	0	0	4
28	78	3	2	5	0	0	4
28	49	2	3	5	0	0	4
28	80	1	1	5	0	0	4
29	66	2	3	5	0	0	4
29	58	3	3	5	0	0	4
29	73	3	3	5	0	0	4
29	73	3	3	5	0	0	4
29	84	3	3	5	0	0	4
29	44	2	3	5	0	0	4
29	69	3	3	5	0	0	4
29	66	2	3	5	0	0	4
29	41	2	3	5	0	0	4
29	41	2	2	5	0	0	4
29	38	2	3	5	0	0	4
29	31	2	0	5	0	0	4
30	52	2	3	5	0	0	4
30	69	2	3	5	0	0	4
30	60	2	3	5	0	0	4
30	59	2	3	5	0	0	4
30	90	3	3	5	0	0	4
30	43	2	3	5	0	0	4
30	42	2	3	5	0	0	4
30	19	2	1	5	0	0	4

```
VAX/VMS  SCRATCH        FOR010 13-OCT-1983 08:25    LPA0:  13-OCT-1983 08:28
VAX/VMS  SCRATCH        FOR010 13-OCT-1983 08:25    LPA0:  13-OCT-1983 08:28
VAX/VMS  SCRATCH        FOR010 13-OCT-1983 08:25    LPA0:  13-OCT-1983 08:28
```

```
 SSSS   CCCC  RRRR     AAA    TTTTT   CCCC  H   H
S      C      R   R   A   A     T    C      H   H
S      C      R   R   A   A     T    C      H   H
 SSS   C      RRRR    A   A     T    C      HHHHH
    S  C      R R     AAAAA     T    C      H   H
    S  C      R  R    A   A     T    C      H   H
SSSS    CCCC  R   R   A   A     T     CCCC  H   H
```

```
FFFFFFFFFF    000000    RRRRRRRR      000000        11        000000
FFFFFFFFFF    000000    RRRRRRRR      000000        11        000000
FF           00    00   RR     RR   00    00     1111      00      00
FF           00    00   RR     RR   00    00     1111      00      00
FF           00    00   RR     RR   00    0000     11      00    0000
FF           00    00   RR     RR   00    0000     11      00    0000
FFFFFFFF     00    00   RRRRRRR     00  00  00     11      00  00  00
FFFFFFFF     00    00   RRRRRRR     00  00  00     11      00  00  00
FF           00    00   RR  RR      0000    00     11      0000    00
FF           00    00   RR  RR      0000    00     11      0000    00
FF           00    00   RR   RR     00      00     11      00      00
FF           00    00   RR   RR     00      00     11      00      00
FF             000000    RR     RR    000000    111111      000000
FF             000000    RR     RR    000000    111111      000000
```

```
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;       11
DDDDDDDD      AAAAAA    TTTTTTTTTT      ;;;;       11
DD      DD   AA    AA      TT          ;;;;      1111
DD      DD   AA    AA      TT          ;;;;      1111
DD      DD   AA    AA      TT                      11
DD      DD   AA    AA      TT                      11
DD      DD   AA    AA      TT          ;;;;        11
DD      DD   AA    AA      TT          ;;;;        11
DD      DD   AAAAAAAAAA    TT          ;;;;        11
DD      DD   AAAAAAAAAA    TT          ;;;;        11
DD      DD   AA    AA      TT            ;;        11
DD      DD   AA    AA      TT            ;;        11
DDDDDDDD     AA    AA      TT          ;;        111111
DDDDDDDD     AA    AA      TT          ;;        111111
```

```
 SSSS   CCCC  RRRR     AAA    TTTTT   CCCC  H   H
S      C      R   R   A   A     T    C      H   H
S      C      R   R   A   A     T    C      H   H
 SSS   C      RRRR    A   A     T    C      HHHHH
    S  C      R R     AAAAA     T    C      H   H
    S  C      R  R    A   A     T    C      H   H
SSSS    CCCC  R   R   A   A     T     CCCC  H   H
```

```
VAX/VMS  SCRATCH        FOR010 13-OCT-1983 08:25    LPA0:  13-OCT-1983 08:28
VAX/VMS  SCRATCH        FOR010 13-OCT-1983 08:25    LPA0:  13-OCT-1983 08:28
VAX/VMS  SCRATCH        FOR010 13-OCT-1983 08:25    LPA0:  13-OCT-1983 08:28
```

```
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  1507. 51407. 01134. 01052. 51232. 01339. 51398. 01439. 01422. 51442. 5
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   460. 5 342. 0 294. 0 278. 5 218. 0 190. 0 157. 0 121. 0  88. 5  70. 5
    55. 5  35. 5  23. 0  13. 0  15. 5   7. 5   6. 0   4. 5   2. 0   0. 5
2 1657. 51552. 01432. 01534. 01421. 01398. 51327. 01228. 51403. 01362. 0
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3 1681. 51642. 01550. 51431. 51533. 01420. 51398. 01326. 51228. 01403. 0
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   890. 0 877. 5 820. 5 788. 5 779. 0 684. 5 649. 0 628. 5 574. 5 519. 0
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6 1640. 01585. 51552. 01662. 01641. 51549. 01429. 51532. 01419. 01398. 0
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```

APPENDIX 7

PROGRAMMES FOR DATA ANALYSIS

RATABLES.FOR

FOR 020

```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K    III    N   N
```

```
RRRRRRRR       AAAAAA     TTTTTTTTTT     AAAAAA     BBBBBBBB     LL           EEEEEEEEEE     SSSSSSSS
RRRRRRRR       AAAAAA     TTTTTTTTTT     AAAAAA     BBBBBBBB     LL           EEEEEEEEEE     SSSSSSSS
RR       RR   AA    AA       TT       AA    AA   BB       BB   LL           EE             SS
RR       RR   AA    AA       TT       AA    AA   BB       BB   LL           EE             SS
RR       RR   AA    AA       TT       AA    AA   BB       BB   LL           EE             SS
RR       RR   AA    AA       TT       AA    AA   BB       BB   LL           EE             SS
RRRRRRRR      AA    AA       TT       AA    AA   BBBBBBBB     LL           EEEEEEEE       SSSSSS
RRRRRRRR      AA    AA       TT       AA    AA   BBBBBBBB     LL           EEEEEEEE       SSSSSS
RR   RR       AAAAAAAAAA     TT       AAAAAAAAAA   BB       BB   LL           EE                   SS
RR   RR       AAAAAAAAAA     TT       AAAAAAAAAA   BB       BB   LL           EE                   SS
RR     RR     AA    AA       TT       AA    AA   BB       BB   LL           EE                   SS
RR     RR     AA    AA       TT       AA    AA   BB       BB   LL           EE                   SS
RR       RR   AA    AA       TT       AA    AA   BBBBBBBB     LLLLLLLLLL   EEEEEEEEEE     SSSSSSSS
RR       RR   AA    AA       TT       AA    AA   BBBBBBBB     LLLLLLLLLL   EEEEEEEEEE     SSSSSSSS
```

```
FFFFFFFFFF     000000     RRRRRRRR        ;;;;       222222         11
FFFFFFFFFF     000000     RRRRRRRR        ;;;;       222222         11
FF            00    00   RR      RR       ;;;;     22      22     1111
FF            00    00   RR      RR       ;;;;     22      22     1111
FF            00    00   RR      RR                      22       11
FF            00    00   RR      RR                      22       11
FFFFFFFF      00    00   RRRRRRRR        ;;;;           22         11
FFFFFFFF      00    00   RRRRRRRR        ;;;;           22         11
FF            00    00   RR  RR          ;;;;         22           11
FF            00    00   RR  RR          ;;;;         22           11
FF            00    00   RR    RR          ;;       22             11
FF            00    00   RR    RR          ;;       22             11
FF              000000     RR      RR      ;;      2222222222     111111
FF              000000     RR      RR      ;;      2222222222     111111
```


```
PPPP     AAA    RRRR    K   K    III    N   N
P   P   A   A   R   R   K   K     I     N   N
P   P   A   A   R   R   K  K      I     NN  N
PPPP    A   A   RRRR    KKK       I     N N N
P       AAAAA   R R     K  K      I     N  NN
P       A   A   R  R    K   K     I     N   N
P       A   A   R   R   K   K    III    N   N
```

```
C*************************************************************************
C                        R A T A B L E S
C      This takes output from S16 (in files FOR008,FOR009,FOR010)
C       and prints tables of incidence and mortality
C       by 5 and 10 year age groups
C       PLUS cumulative person-years of life lost each year
C*************************************************************************
       DIMENSION IDEAD(30,100),ICASE(30,100),PYS(30,100)
       DIMENSION IVDEAD(10,20),IVCASE(10,20)
       DIMENSION IXDEAD(10,10),IXCASE(10,10)
       DIMENSION ITDEAD(10),   ITCASE(10)
       DIMENSION VDEAD(10,20),VCASE(10,20),VPYS(10,20)
       DIMENSION XDEAD(10,10),XCASE(10,10),XPYS(10,10)
       DIMENSION TDEAD(10),   TCASE(10),   TPYS(10)
       DIMENSION VDRATE(10,20),VIRATE(10,20)
       DIMENSION XDRATE(10,10),XIRATE(10,10)
       DIMENSION TDRATE(10),   TIRATE(10)
       DIMENSION IYRTABS(10)
       DIMENSION IMAXAGE(10),IYRSLEFT(7)
       DIMENSION LFYRDAT(100),IPYLL(30)
C*************************************************************************
C DATA IS YEARS FOR WHICH TABLES ARE REQUIRED EG. 10 = 1961-70, 20=1971-80
C*************************************************************************
       DATA IYRTABS/30,10,20,30,5,10,15,20,25,30/
C*************************************************************************
C DATA FOR LIFE TABLE EXPECTATION OF LIFE.....2 FORMATS!
C IMAXAGE IS MAX AGE REACHED AT AGES GIVEN e.g. 1-39=77,40-51=78,etc
C IYRSLEFT IS e0x AT AGES GIVEN e.g.80-82=7,83-84=6,...etc
C*************************************************************************
       DATA IMAXAGE/39,51,59,63,67,70,73,76,77,79/
       DATA IYRSLEFT/82,84,87,91,95,98,100/
C*************************************************************************
C  READ IN DATA FILES
C*************************************************************************
    5  READ(8,801,END=10) IYR,IAG
       IDEAD(IYR,IAG) = IDEAD(IYR,IAG) + 1
       GO TO 5
   10  READ(9,801,END=20) IYR,IAG
       ICASE(IYR,IAG) = ICASE(IYR,IAG) + 1
       GO TO 10
   20  DO 30 I=1,30
          DO 25 J = 1,10
          IU = J * 10
          IL = IU - 9
          READ(10,1001) (PYS(I,IAG),IAG = IL,IU)
   25     CONTINUE
   30  CONTINUE
C*************************************************************************
C DRAW UP oEx ARRAY LFRYDAT(i.e. VALUE FOR EACH YEAR) FROM DATA GIVEN
C*************************************************************************
       ICOUNT = 1
       DO 42 I=1,10
         DO 40 J=ICOUNT,IMAXAGE(I)
         LFYRDAT(J)= (77 + I) - J
   40    CONTINUE
       ICOUNT = IMAXAGE(I) + 1
   42  CONTINUE
       DO 46 I=1,7
         DO 44 J = ICOUNT,IYRSLEFT(I)
         LFYRDAT(J) = 8 - I
   44    CONTINUE
```

```
      ICOUNT = IYRSLEFT(I) + 1
   46 CONTINUE
C*************************************************************************
C  CALCULATE & PRINT RATES FOR PERIODS DEFINED BY IYRTABS
C*************************************************************************
      K=0
      DO 500 I = 1,10
      IF (IYRTABS(I).EQ.0) GO TO 600
      K = K + 1
       IF (K .LT. 31) GOTO 50
       K = 1
   50   IYR1 = 1960 + K
        IYR2 = 1960 + IYRTABS(I)
        WRITE(20,601) IYR1,IYR2
        WRITE(20,602)
C*************************************************************************
C  5 YEAR AGE GROUP TABLES
C*************************************************************************
          DO 200 N = 1,20
          IUA = N * 5
          ILA = IUA - 4
          IPL = ILA - 1
          IPU = IUA - 1
              DO 150 J = K,IYRTABS(I)
                   DO 120 M = ILA,IUA
                   IVDEAD(I,N) = IVDEAD(I,N) + IDEAD(J,M)
                   IVCASE(I,N) = IVCASE(I,N) + ICASE(J,M)
                   VPYS(I,N)   = VPYS(I,N) + PYS(J,M)
  120              CONTINUE
  150         CONTINUE
          VDEAD(I,N) = FLOAT(IVDEAD(I,N))
          IF(VDEAD(I,N).GT.0.0) GOTO 160
          VDRATE(I,N) = 0.0
          GOTO 170
  160     VDRATE(I,N) = (VDEAD(I,N) * 100000) / VPYS(I,N)
  170     VCASE(I,N) = FLOAT(IVCASE(I,N))
          IF(VCASE(I,N).GT.0.0) GOTO 180
          VIRATE(I,N) = 0.0
          GO TO 190
  180     VIRATE(I,N) = (VCASE(I,N) * 100000) / VPYS(I,N)
  190     WRITE(20,2001)IPL,IPU,IVCASE(I,N),VIRATE(I,N),IVDEAD(I,N),
     1    VDRATE(I,N)
  200     CONTINUE
C*************************************************************************
C TABLES FOR 10 YEAR AGEGROUPS
C*************************************************************************
          WRITE(20,602)
          DO 300 N = 1,10
          IUA = N*10
          ILA = IUA - 9
          IPL = ILA - 1
          IPU = IUA - 1
             DO 250 J = K,IYRTABS(I)
                   DO 220 M = ILA,IUA
                   IXDEAD(I,N) = IXDEAD(I,N) + IDEAD(J,M)
                   IXCASE(I,N) = IXCASE(I,N) + ICASE(J,M)
                   XPYS(I,N)   = XPYS(I,N) + PYS(J,M)
  220              CONTINUE
  250         CONTINUE
          XDEAD(I,N) = FLOAT(IXDEAD(I,N))
          IF(XDEAD(I,N).GT.0.0) GOTO 260
```

```
            XDRATE(I,N) = 0.0
            GOTO 270
  260       XDRATE(I,N) = (XDEAD(I,N) * 100000) / XPYS(I,N)
  270       XCASE(I,N) = FLOAT(IXCASE(I,N))
            IF(XCASE(I,N).GT.0.0) GOTO 280
            XIRATE(I,N) = 0.0
            GO TO 290
  280       XIRATE(I,N) = (XCASE(I,N) * 100000) / XPYS(I,N)
  290       WRITE(20,2001)IPL,IPU,IXCASE(I,N),XIRATE(I,N),IXDEAD(I,N),
     1      XDRATE(I,N)
  300       CONTINUE
C*************************************************************************
C CALCULATE NOS. AND RATES FOR ALL AGES
C*************************************************************************
            WRITE(20,602)
            DO 350 J = K,IYRTABS(I)
                 DO 320 M = 1,100
                 ITDEAD(I) = ITDEAD(I) + IDEAD(J,M)
                 ITCASE(I) = ITCASE(I) + ICASE(J,M)
                 TPYS(I)   = TPYS(I) + PYS(J,M)
  320            CONTINUE
  350       CONTINUE
            TDEAD(I) = FLOAT(ITDEAD(I))
            IF(TDEAD(I).GT.0.0) GOTO 360
            TDRATE(I) = 0.0
            GOTO 370
  360       TDRATE(I) = (TDEAD(I) * 100000) / TPYS(I)
  370       TCASE(I) = FLOAT(ITCASE(I))
            IF(TCASE(I) .GT.  0.0) GOTO 380
            TCASE(I) = 0.0
            GO TO 390
  380       TIRATE(I) = (TCASE(I) * 100000) / TPYS(I)
  390       WRITE(20,2002) ITCASE(I),TIRATE(I),ITDEAD(I),TDRATE(I)
          K = IYRTABS(I)
  500     CONTINUE
C*************************************************************************
C WRITE OUT CUMULATIVE LIFE YEARS LOST AT EACH YEAR
C*************************************************************************
          WRITE(20,603)
          DO 520 I = 1,30
            DO 510 J = 1,100
            IPYLL(I) = IPYLL(I) + (IDEAD(I,J)*LFYRDAT(J))
  510       CONTINUE
          WRITE(20,2003) I,IPYLL(I)
          IPYLL(I+1) = IPYLL(I)
  520     CONTINUE
  600     STOP
  601     FORMAT(/,3X,'YEARS  ',I4,' TO ',I4)
  602     FORMAT(/,3X,'AGE',3X,'CASES',3X,'INC',2X,'DEATHS',2X,'RATE')
  603     FORMAT(/,2X,'YEAR',2X,'P-YRS LOST')
  801     FORMAT(2I3)
 1001     FORMAT(4X,10(F6.1))
 2001     FORMAT(1X,I2,' - ',I2,2(1X,I4,1X,F7.2))
 2002     FORMAT(1X,'ALL AGE',2(1X,I4,1X,F7.2))
 2003     FORMAT(3X,I2,5X,I7)
          END
```

```
VAX/VMS  SCRATCH      FOR020 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:29
VAX/VMS  SCRATCH      FOR020 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:29
VAX/VMS  SCRATCH      FOR020 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:29
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
FFFFFFFFFF    000000    RRRRRRRR      000000      222222      000000
FFFFFFFFFF    000000    RRRRRRRR      000000      222222      000000
FF           00    00   RR     RR   00    00   22    22   00    00
FF           00    00   RR     RR   00    00   22    22   00    00
FF           00    00   RR     RR   00  0000         22   00  0000
FF           00    00   RR     RR   00  0000         22   00  0000
FFFFFFFF     00    00   RRRRRRRR    00 00 00       22     00 00 00
FFFFFFFF     00    00   RRRRRRRR    00 00 00       22     00 00 00
FF           00    00   RR  RR      0000   00     22      0000   00
FF           00    00   RR  RR      0000   00     22      0000   00
FF           00    00   RR   RR    00     00   22        00     00
FF           00    00   RR   RR    00     00   22        00     00
FF             000000    RR     RR   000000   2222222222   000000
FF             000000    RR     RR   000000   2222222222   000000
```

```
DDDDDDDD      AAAAAA     TTTTTTTTTT      ;;;;       11
DDDDDDDD      AAAAAA     TTTTTTTTTT      ;;;;       11
DD      DD   AA    AA       TT           ;;;;     1111
DD      DD   AA    AA       TT           ;;;;     1111
DD      DD   AA    AA       TT                      11
DD      DD   AA    AA       TT                      11
DD      DD   AA    AA       TT           ;;;;       11
DD      DD   AA    AA       TT           ;;;;       11
DD      DD   AAAAAAAAAA     TT           ;;;;       11
DD      DD   AAAAAAAAAA     TT           ;;;;       11
DD      DD   AA    AA       TT             ;;       11
DD      DD   AA    AA       TT             ;;       11
DDDDDDDD     AA    AA       TT           ;;       111111
DDDDDDDD     AA    AA       TT           ;;       111111
```

```
 SSSS   CCCC  RRRR    AAA   TTTTT   CCCC  H   H
S      C      R   R  A   A    T    C      H   H
S      C      R   R  A   A    T    C      H   H
 SSS   C      RRRR   A   A    T    C      HHHHH
    S  C      R R    AAAAA    T    C      H   H
    S  C      R  R   A   A    T    C      H   H
SSSS    CCCC  R   R  A   A    T     CCCC  H   H
```

```
VAX/VMS  SCRATCH      FOR020 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:29
VAX/VMS  SCRATCH      FOR020 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:29
VAX/VMS  SCRATCH      FOR020 13-OCT-1983 08:25   LPA0:  13-OCT-1983 08:29
```

YEARS 1961 TO 1990

AGE	CASES	INC	DEATHS	RATE
0 - 4	0	0.00	0	0.00
5 - 9	0	0.00	0	0.00
10 - 14	0	0.00	0	0.00
15 - 19	1	0.45	0	0.00
20 - 24	2	0.93	0	0.00
25 - 29	10	4.89	5	2.44
30 - 34	26	13.23	3	1.53
35 - 39	25	12.86	6	3.09
40 - 44	51	26.54	20	10.41
45 - 49	56	29.94	17	9.09
50 - 54	46	24.45	41	21.79
55 - 59	55	29.50	34	18.23
60 - 64	38	21.21	32	17.87
65 - 69	40	24.44	27	16.50
70 - 74	52	37.39	41	29.48
75 - 79	28	26.38	24	22.61
80 - 84	23	34.80	25	37.83
85 - 89	10	31.84	9	28.66
90 - 94	1	9.96	4	39.84
95 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
0 - 9	0	0.00	0	0.00
10 - 19	1	0.23	0	0.00
20 - 29	12	2.86	5	1.19
30 - 39	51	13.05	9	2.30
40 - 49	107	28.22	37	9.76
50 - 59	101	26.96	75	20.02
60 - 69	78	22.75	59	17.21
70 - 79	80	32.62	65	26.51
80 - 89	33	33.85	34	34.88
90 - 99	1	8.58	4	34.33

AGE	CASES	INC	DEATHS	RATE
ALL AGE	464	14.87	288	9.23

YEARS 1961 TO 1970

AGE	CASES	INC	DEATHS	RATE
0 - 4	0	0.00	0	0.00
5 - 9	0	0.00	0	0.00
10 - 14	0	0.00	0	0.00
15 - 19	0	0.00	0	0.00
20 - 24	1	1.49	0	0.00
25 - 29	3	4.90	1	1.63
30 - 34	9	14.78	0	0.00
35 - 39	8	12.71	1	1.59
40 - 44	21	31.78	10	15.13
45 - 49	21	31.83	7	10.61
50 - 54	23	34.56	18	27.05
55 - 59	21	31.77	16	24.20
60 - 64	24	40.25	11	18.45
65 - 69	14	27.40	8	15.66
70 - 74	23	55.02	14	33.49
75 - 79	9	29.28	8	26.03
80 - 84	3	16.22	2	10.82
85 - 89	3	37.19	1	12.40

90 - 94	1	46.01	1	46.01
95 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
0 - 9	0	0.00	0	0.00
10 - 19	0	0.00	0	0.00
20 - 29	4	3.12	1	0.78
30 - 39	17	13.73	1	0.81
40 - 49	42	31.80	17	12.87
50 - 59	44	33.17	34	25.63
60 - 69	38	34.32	19	17.16
70 - 79	32	44.11	22	30.33
80 - 89	6	22.59	3	11.30
90 - 99	1	40.96	1	40.96

AGE	CASES	INC	DEATHS	RATE
ALL AGE	184	18.00	98	9.59

YEARS 1971 TO 1980

AGE	CASES	INC	DEATHS	RATE
0 - 4	0	0.00	0	0.00
5 - 9	0	0.00	0	0.00
10 - 14	0	0.00	0	0.00
15 - 19	0	0.00	0	0.00
20 - 24	1	1.44	0	0.00
25 - 29	5	7.02	4	5.62
30 - 34	8	11.98	3	4.49
35 - 39	12	19.75	2	3.29
40 - 44	14	23.30	3	4.99
45 - 49	16	25.99	3	4.87
50 - 54	8	12.56	8	12.56
55 - 59	18	28.90	11	17.66
60 - 64	5	8.19	7	11.46
65 - 69	16	27.63	11	18.99
70 - 74	16	33.38	14	29.21
75 - 79	9	25.51	7	19.84
80 - 84	14	63.11	15	67.61
85 - 89	4	36.99	4	36.99
90 - 94	0	0.00	3	82.77
95 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
0 - 9	0	0.00	0	0.00
10 - 19	0	0.00	0	0.00
20 - 29	6	4.27	4	2.85
30 - 39	20	15.68	5	3.92
40 - 49	30	24.66	6	4.93
50 - 59	26	20.64	19	15.08
60 - 69	21	17.65	18	15.13
70 - 79	25	30.05	21	25.24
80 - 89	18	54.55	19	57.58
90 - 99	0	0.00	3	71.92

AGE	CASES	INC	DEATHS	RATE
ALL AGE	146	13.92	95	9.05

YEARS 1981 TO 1990

AGE	CASES	INC	DEATHS	RATE
0 - 4	0	0.00	0	0.00

5 - 9	0	0.00	0	0.00
10 - 14	0	0.00	0	0.00
15 - 19	1	1.30	0	0.00
20 - 24	0	0.00	0	0.00
25 - 29	2	2.77	0	0.00
30 - 34	9	13.08	0	0.00
35 - 39	5	7.08	3	4.25
40 - 44	16	24.25	7	10.61
45 - 49	19	31.93	7	11.76
50 - 54	15	25.91	15	25.91
55 - 59	16	27.54	7	12.05
60 - 64	9	15.40	14	23.96
65 - 69	10	18.29	8	14.63
70 - 74	13	26.34	13	26.34
75 - 79	10	24.93	9	22.43
80 - 84	6	23.61	8	31.48
85 - 89	3	23.96	4	31.94
90 - 94	0	0.00	0	0.00
95 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
0 - 9	0	0.00	0	0.00
10 - 19	1	0.70	0	0.00
20 - 29	2	1.33	0	0.00
30 - 39	14	10.04	3	2.15
40 - 49	35	27.89	14	11.16
50 - 59	31	26.73	22	18.97
60 - 69	19	16.80	22	19.45
70 - 79	23	25.71	22	24.59
80 - 89	9	23.73	12	31.63
90 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
ALL AGE	134	12.78	95	9.06

YEARS 1961 TO 1965

AGE	CASES	INC	DEATHS	RATE
0 - 4	0	0.00	0	0.00
5 - 9	0	0.00	0	0.00
10 - 14	0	0.00	0	0.00
15 - 19	0	0.00	0	0.00
20 - 24	0	0.00	0	0.00
25 - 29	1	3.30	0	0.00
30 - 34	4	13.02	0	0.00
35 - 39	6	18.54	1	3.09
40 - 44	14	41.24	4	11.78
45 - 49	13	40.03	4	12.32
50 - 54	18	51.71	10	28.73
55 - 59	14	43.16	6	18.50
60 - 64	12	41.74	7	24.35
65 - 69	7	28.45	3	12.19
70 - 74	13	63.97	5	24.61
75 - 79	5	33.86	5	33.86
80 - 84	1	11.67	0	0.00
85 - 89	0	0.00	0	0.00
90 - 94	0	0.00	1	115.07
95 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
0 - 9	0	0.00	0	0.00

10 - 19	0	0.00	0	0.00
20 - 29	1	1.63	0	0.00
30 - 39	10	15.85	1	1.58
40 - 49	27	40.65	8	12.04
50 - 59	32	47.59	16	23.79
60 - 69	19	35.61	10	18.74
70 - 79	18	51.30	10	28.50
80 - 89	1	8.27	0	0.00
90 - 99	0	0.00	1	101.73

AGE	CASES	INC	DEATHS	RATE
ALL AGE	108	21.43	46	9.13

YEARS 1966 TO 1970

AGE	CASES	INC	DEATHS	RATE
0 - 4	0	0.00	0	0.00
5 - 9	0	0.00	0	0.00
10 - 14	0	0.00	0	0.00
15 - 19	0	0.00	0	0.00
20 - 24	1	2.77	0	0.00
25 - 29	2	6.46	1	3.23
30 - 34	5	16.57	0	0.00
35 - 39	2	6.54	0	0.00
40 - 44	7	21.78	6	18.67
45 - 49	8	23.88	3	8.95
50 - 54	5	15.75	8	25.20
55 - 59	7	20.79	10	29.70
60 - 64	12	38.86	4	12.95
65 - 69	7	26.42	5	18.87
70 - 74	10	46.54	9	41.89
75 - 79	4	25.04	3	18.78
80 - 84	2	20.17	2	20.17
85 - 89	3	65.62	1	21.87
90 - 94	1	76.66	0	0.00
95 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
0 - 9	0	0.00	0	0.00
10 - 19	0	0.00	0	0.00
20 - 29	3	4.47	1	1.49
30 - 39	7	11.52	0	0.00
40 - 49	15	22.85	9	13.71
50 - 59	12	18.34	18	27.52
60 - 69	19	33.12	9	15.69
70 - 79	14	37.38	12	32.04
80 - 89	5	34.51	3	20.70
90 - 99	1	68.56	0	0.00

AGE	CASES	INC	DEATHS	RATE
ALL AGE	76	14.67	52	10.04

YEARS 1971 TO 1975

AGE	CASES	INC	DEATHS	RATE
0 - 4	0	0.00	0	0.00
5 - 9	0	0.00	0	0.00
10 - 14	0	0.00	0	0.00
15 - 19	0	0.00	0	0.00
20 - 24	1	2.84	0	0.00
25 - 29	4	11.11	2	5.55

30 - 34	7	22.66	2	6.48
35 - 39	5	16.66	2	6.66
40 - 44	9	29.68	0	0.00
45 - 49	7	22.10	1	3.16
50 - 54	2	6.10	4	12.21
55 - 59	9	29.41	3	9.80
60 - 64	4	12.51	4	12.51
65 - 69	6	21.07	5	17.55
70 - 74	10	43.29	8	34.63
75 - 79	3	17.65	4	23.53
80 - 84	7	65.07	5	46.48
85 - 89	3	58.42	3	58.42
90 - 94	0	0.00	3	174.37
95 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
0 - 9	0	0.00	0	0.00
10 - 19	0	0.00	0	0.00
20 - 29	5	7.02	2	2.81
30 - 39	12	19.70	4	6.57
40 - 49	16	25.81	1	1.61
50 - 59	11	17.36	7	11.05
60 - 69	10	16.54	9	14.89
70 - 79	13	32.42	12	29.93
80 - 89	10	62.92	8	50.34
90 - 99	0	0.00	3	154.36

AGE	CASES	INC	DEATHS	RATE
ALL AGE	77	14.65	46	8.75

YEARS 1976 TO 1980

AGE	CASES	INC	DEATHS	RATE
0 - 4	0	0.00	0	0.00
5 - 9	0	0.00	0	0.00
10 - 14	0	0.00	0	0.00
15 - 19	0	0.00	0	0.00
20 - 24	0	0.00	0	0.00
25 - 29	1	2.84	2	5.69
30 - 34	1	2.78	1	2.78
35 - 39	7	22.77	0	0.00
40 - 44	5	16.80	3	10.08
45 - 49	9	30.11	2	6.69
50 - 54	6	19.40	4	12.93
55 - 59	9	28.41	8	25.26
60 - 64	1	3.44	3	10.31
65 - 69	10	33.98	6	20.39
70 - 74	6	24.16	6	24.16
75 - 79	6	32.83	3	16.41
80 - 84	7	61.25	10	87.50
85 - 89	1	17.61	1	17.61
90 - 94	0	0.00	0	0.00
95 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
0 - 9	0	0.00	0	0.00
10 - 19	0	0.00	0	0.00
20 - 29	1	1.45	2	2.89
30 - 39	8	12.00	1	1.50
40 - 49	14	23.47	5	8.38
50 - 59	15	23.96	12	19.17

60 - 69	11	18.79	9	15.38
70 - 79	12	27.84	9	20.88
80 - 89	8	46.76	11	64.30
90 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
ALL AGE	69	13.18	49	9.36

YEARS 1981 TO 1985

AGE	CASES	INC	DEATHS	RATE
0 - 4	0	0.00	0	0.00
5 - 9	0	0.00	0	0.00
10 - 14	0	0.00	0	0.00
15 - 19	0	0.00	0	0.00
20 - 24	0	0.00	0	0.00
25 - 29	1	2.95	0	0.00
30 - 34	6	17.12	0	0.00
35 - 39	3	8.39	1	2.80
40 - 44	7	22.94	5	16.38
45 - 49	12	40.85	3	10.21
50 - 54	10	34.26	3	10.28
55 - 59	7	23.46	5	16.76
60 - 64	5	16.64	5	16.64
65 - 69	1	3.72	2	7.44
70 - 74	7	27.14	7	27.14
75 - 79	5	25.59	6	30.71
80 - 84	3	24.35	2	16.24
85 - 89	2	33.20	1	16.60
90 - 94	0	0.00	0	0.00
95 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
0 - 9	0	0.00	0	0.00
10 - 19	0	0.00	0	0.00
20 - 29	1	1.38	0	0.00
30 - 39	9	12.71	1	1.41
40 - 49	19	31.72	8	13.36
50 - 59	17	28.80	8	13.56
60 - 69	6	10.54	7	12.30
70 - 79	12	26.47	13	28.68
80 - 89	5	27.26	3	16.36
90 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
ALL AGE	69	13.19	40	7.64

YEARS 1986 TO 1990

AGE	CASES	INC	DEATHS	RATE
0 - 4	0	0.00	0	0.00
5 - 9	0	0.00	0	0.00
10 - 14	0	0.00	0	0.00
15 - 19	1	2.74	0	0.00
20 - 24	0	0.00	0	0.00
25 - 29	1	2.62	0	0.00
30 - 34	3	8.88	0	0.00
35 - 39	2	5.73	2	5.73
40 - 44	9	25.38	2	5.64
45 - 49	7	23.23	4	13.27
50 - 54	5	17.41	12	41.79

55 - 59	9	31.85	2	7.08
60 - 64	4	14.10	9	31.72
65 - 69	9	32.35	6	21.57
70 - 74	6	25.47	6	25.47
75 - 79	5	24.29	3	14.58
80 - 84	3	22.91	6	45.83
85 - 89	1	15.39	3	46.16
90 - 94	0	0.00	0	0.00
95 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
0 - 9	0	0.00	0	0.00
10 - 19	1	1.52	0	0.00
20 - 29	1	1.28	0	0.00
30 - 39	5	7.28	2	2.91
40 - 49	16	24.40	6	9.15
50 - 59	14	24.58	14	24.58
60 - 69	13	23.13	15	26.69
70 - 79	11	24.92	9	20.39
80 - 89	4	20.42	9	45.94
90 - 99	0	0.00	0	0.00

AGE	CASES	INC	DEATHS	RATE
ALL AGE	65	12.37	55	10.47

YEAR	P-YRS LOST
1	151
2	235
3	504
4	750
5	966
6	1274
7	1507
8	1639
9	1909
10	2056
11	2203
12	2444
13	2542
14	2675
15	2856
16	3061
17	3245
18	3417
19	3643
20	3771
21	3973
22	4089
23	4168
24	4313
25	4539
26	4665
27	5002
28	5217
29	5476
30	5573